JSC 20483
Revision B

JSC INSTITUTIONAL REVIEW BOARD
GUIDELINES FOR INVESTIGATORS PROPOSING HUMAN RESEARCH FOR SPACE FLIGHT AND RELATED INVESTIGATIONS

Space and Life Science Directorate

July 1996

National Aeronautics
and Space Administration

Lyndon B. Johnson Space Center
Houston, TX

JSC Institutional Review Board

Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations

Approved by: _____ 17 June 1996
L. F. Dietlein, M.D., Ph.D. Date
Chairperson, JSC Institutional Review Board

Concurrence: _____ 6/15/96
H. David Short, M.D. Date
Director, Space & Life Sciences

Concurrence: _____ 6/26/96
D. C. Leestma Date
Director, Flight Crew Operations

Table of Contents

This page intentionally left blank.

Acronyms and Abbreviations

f	Frequency
μA	Microampere
a.c.	Alternating Current
AAALAC	American Association for Accreditation of Laboratory Animal Care
AAMI	Association for the Advancement of Medical Instrumentation
ACES	Advanced Crew Escape Suit
ACHRE	Advisory Committee for Human Research Experiments
ACLS	Advanced Cardiac Life Support
ALARA	As Low As Reasonably Achievable
ANSI	American National Standards Institute
AO	Announcement of Opportunity
BDC	Baseline Data Collection
BLS	Basic Life Support
Board	JSC Institutional Review Board
cc	Cubic Centimeter
CDR	Commander (of Space Shuttle)
Center	Lyndon B. Johnson Space Center
CFR	Code of Federal Regulations
Co-I	Co-Investigator
d.c.	Direct Current
DHEW	Department of Health, Education, and Welfare (now: Department of Health and Human Services (DHHS)
DHHS	Department of Health and Human Services
DMO	Designated Medical Officer
DSO	Detailed Supplementary Objective
DTO	Development Test Objective
DTP	Detailed Test Procedure
ECG	Electrocardiogram, Electrocardiography
EMG	Electromyogram, Electromyography
EMU	External Maneuvering Unit
EOG	Electro-oculogram
EVA	Extravehicular Activity
FDA	Food and Drug Administration
FRR	Flight Readiness Review
GPWS	General Purpose Work Station
HEPA	High Efficiency Particulate Air
HERD	Human Experimental and Research Data Records
HIMS	Health Information Management System
HRPPC	Human Research Policy and Procedures Committee (predecessor to JSC IRB)
HSEC	Health, Safety, and Environmental Compliance Officer
IDE	Investigational Device Exemption
IEC	International Electrotechnical Commission
IND	Investigational New Drug
IRB	Institutional Review Board

ISS	International Space Station
JHB	Johnson Space Center Handbook
JMI	Johnson Space Center Management Instruction
JPD	Johnson Space Center Policy Directive
JSC	Lyndon B. Johnson Space Center
KC-135	NASA Zero-G Aircraft (Parabolic Flight)
kg	Kilogram
kHz	Kilohertz
LBNP	Lower Body Negative Pressure
LCG	Liquid Cooled Garment
LD50	Lethal Dose-50
LES	Launch/Entry Suit (Launch Escape Suit)
mA	Milliampere
Mir	Russian Space Station
MOCR	Mission Operations Control Room
MPA	Multiple Project Assurance
MS	Mission Specialist (of Space Shuttle)
NASA	National Aeronautics and Space Administration
NFPA	National Fire Protection Association
NFQ	NASA Flight Quality
NIH	National Institutes of Health
NMI	NASA Management Instruction
NRA	NASA Research Announcement
NRC	Nuclear Regulatory Commission
NSTS	National Space Transportation System (no longer used)
OFT	Orbital Flight Test
OPRR	Office for Protection from Research Risks
ORR	Operational Readiness Review
OSTP	Office of Science and Technology Policy
PCO	Protocol Compliance Officer
PHS	Public Health Service
PI	Principal Investigator
PLT	Pilot (of Space Shuttle)
PPO	Policy and Procedure Order
PS	Payload Specialist (of Space Shuttle)
PSRP	Payload Safety Review Panel
RAHF	Research Animal Holding Facility
RCP	Radiation Constraints Panel
RDRC	Radioactive Drug Research Committee
RPWG	Radioactive Payloads Working Group
RSA	Russian Space Agency
RSC	Radiation Safety Committee
S&LSD	Space and Life Sciences Directorate
SBRI	Space Biomedical Research Institute
SMART	Safety and Mission Assurance Review Team
SMRC	Scientific Merit Review Committee
SPA	Single Project Assurance
SR&QA	Safety, Reliability, and Quality Assurance
SR&T	Scientific Research and Technology

STS	Space Transportation System
TC	Test Conductor
TD	Test Director
TRR	Test Readiness Review
TRRB	Test Readiness Review Board
UL	Underwriters Laboratories, Inc.

This page intentionally left blank.

Glossary

Co-Investigator - a scientist who works closely with the Principal Investigator on flight experiments that have been selected for a specific mission or on ground-based studies which support flight experiments.

Crew Surgeon - a flight surgeon assigned to a particular mission. The crew surgeon is responsible for maintaining the overall health of the astronauts of a given mission.

Human Test Subject Facility Recruiter - the individual responsible for locating suitable test subjects for JSC IRB approved ground-based experiments.

Medical Monitor - a physician or other technically qualified individual appointed by the JSC IRB to monitor experiments to ensure compliance with Board requirements. The qualifications and certifications required of the medical monitor(s) are determined by the JSC IRB.

Mission Scientist - the NASA science supervisor responsible for the overall scientific conduct of the mission.

Mission Manager - the NASA management supervisor responsible for the overall development, integration, and operation of all aspects the mission payload.

NASA Test Director - the individual with the overall responsibility for and authority over a ground-based test. The test director is responsible for all aspects of test safety.

Principal Investigator - a scientist whose proposed flight experiment has been selected for a specific mission or ground-based study.

Project Scientist - the NASA field center scientist/manager responsible for the detailed development/integration of flight experiments, for representing the interests of selected investigators, and for interfacing their experiments with the various mission organizations.

Protocol Compliance Officer - a medical monitor whose primary function is to verify that all experiments are conducted in accordance with IRB requirements and ethical principles. The PCO is not a member of the JSC IRB.

Secretary/Recorder - the individual who provides clerical support to the JSC IRB by ensuring the collection of accurate records and the publication of JSC IRB activities, including agendas, proceedings, and action items. The Secretary/Recorder is not a member of the JSC IRB but serves as a point-of-contact for investigators submitting protocols to the JSC IRB for review, and for annual renewal of protocol approval.

This page intentionally left blank.

Points-of-Contact

Chairperson, JSC IRB	Lawrence Dietlein, M.D., Ph.D. Mail Code: SA Tel: (713) 483-6291 Fax: (713) 483-6089
Alternate Chairperson, JSC IRB	Charles Sawin, Ph.D. Mail Code: SD5 Tel: (713) 483-7202 Fax: (713) 244-5734
Secretary/Recorder	Ms. Mary Flores Mail Code: KRUG PM/P2 Tel: (713) 212-1468 Fax: (713) 212-1465
Chairperson, Payload Safety Review Panel (Flight equipment only)	Mr. Harold Battaglia Mail Code: MA2 Tel: (713) 483-1159 Fax: (713) 483-5389
Chairperson, JSC Radiation Safety Committee	Douglas Blanchard, Ph.D. Mail Code: SN Tel: (713) 483-5151 Fax: (713) 244-8892
Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee	Tracy Yang, Ph.D. Mail Code: SD4 Tel: (713) 483-5583 Fax: (713) 483-3058
JSC Radiation Constraints Panel	Tracy Yang, Ph.D. Mail Code: SD4 Tel: (713) 483-5583 Fax: (713) 483-3058
Scientific Merit Review Committee	Lawrence Dietlein, M.D., Ph.D. Mail Code: SA Tel: (713) 483-6291 Fax: (713) 483-6089
Protocol Compliance Officer	Terrence Pattinson, M.D. Mail Code: SD2 Tel: (713) 483-8142 Fax: (713) 244-5734 Beeper: (713) 891-7841

Safety, Reliability, and Quality Assurance Office - Health, Safety & Environmental Compliance Office (Ground-based equipment only)	Mr. Wayne Gremillion Mail Code: NA3 Tel: (713) 483-4287 Fax: (713) 244-2318

Internet Access

Individuals with NASA/JSC Internet privileges may access portions of this document electronically by following the steps below:

1. Locate the JSC Home Page by typing "http://www.jsc.nasa.gov" (without the quotes).

2. Click on "Internal JSC Home Page". Once at the Internal JSC Home Page:

    2a. Click on "Management Directives" to locate JSC Management Instructions (also known as Policy Directives), and JSC Handbooks (Guidelines);

    2b. Click on "Scientific & Technical Information Center" to obtain JSC Forms.

This page intentionally left blank.

INTRODUCTION

This document is intended to provide investigators with a thorough understanding of the Lyndon B. Johnson Space Center (JSC) Institutional Review Board (IRB) function. In addition, the process of submitting a research protocol for consideration and the methods of monitoring the research protocol for safety and compliance are defined. The authority and scope of the JSC IRB, its charter, some definitions, and the ethical principles which guide the Board are described.

1.0 OVERVIEW OF THE JSC IRB

1.1 Guiding Principles of the JSC IRB

A. Human research must always be based on fundamental ethical principles. These principles include the following: 1) Experiments are performed only on persons who freely volunteer for the research, without coercion in any form; 2) A subject may withdraw from an experiment at any time, for any reason, without penalty. The Federal policy for the protection of human research subjects, referred to as the "Common Rule" (45 CFR Part 46, Subpart A) establishes the ethical framework for all federally funded human research. A brief overview of the policy is given in Appendix A. Additional guidelines describing basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects may be found in Appendix B.

B. Coercion to participate in research can take many forms and must be diligently avoided. There can be no agreements that imply consent prior to being informed of the detailed risks of the experiment. The Principal Investigator (PI) has the primary responsibility for the safe and ethical conduct of human experiments. The JSC IRB is the oversight organization charged with assuring the health, safety, and well-being of human research subjects in any JSC investigation or NASA-sponsored space flight investigation.

1.2 Charter of the JSC IRB

A. Research protocols using human test subjects must be approved by the NASA - JSC IRB when research is conducted in spacecraft, NASA-JSC facilities, NASA-JSC aircraft, or at other centers or institutions when JSC civil service or contractor personnel are directly involved in the research activities. All research involving space flight crews must be approved by the JSC IRB. JSC-funded human research at all other institutions in which no JSC civil service or contractor personnel participation is directly involved shall be reviewed by the IRB of the institution performing the research. The authority for and responsibilities of this Board derive from JHB 1107.1 (Appendix C) and NASA Management Instruction (NMI) 7100.8 (Appendix D).

B. Most institutions will require that their own IRB review research protocols involving test subjects at their institutions. Such a review does not obviate the

review by the JSC IRB. This duplication of effort is unavoidable because two different sets of requirements must be met.

1.3 Composition of the JSC IRB

A. The *minimum* membership of the JSC IRB is:

- The Chairperson
- An Alternate Chairperson (Executive Secretary)
- A life scientist
- A flight surgeon
- A representative from the Legal Office
- A representative from the Safety, Reliability, and Quality Assurance (SR&QA) Office
- An astronaut
- A non-life-sciences employee
- A non-NASA, full-time Federal employee

B. Members of the Board are appointed by the Center Director and are Federal employees. Members are expected to attend regularly. At least one third of the membership will be physicians. Up to three ad hoc members in specialized disciplines may be added to the JSC IRB on a temporary, non-voting basis as deemed appropriate by the Chairperson (Appendices C and D). The member position filled by a non-life-sciences employee will be rotated among the Center Directorates and Offices.

C. The permanent Chairperson will periodically designate a Board member as acting Chairperson to afford experience in conducting the meetings while the former will retain overall control of the standing Board.

D. All members of the JSC IRB are voting members. The Chairperson will vote only in the event of a tie. A majority of JSC IRB members present is required to evaluate and approve a protocol and must include the Chairperson (or alternate Chairperson) and representatives of the Astronaut Office (a representative of the Astronaut Office is required for evaluation of flight studies), SR&QA Office, and Medical Operations. Every member is required to vote on each issue except in conflict of interest cases or when lack of technical familiarity with aspects of a protocol would render that vote inappropriate.

1.4 Working Principles of the JSC IRB

A. The JSC IRB meets regularly and uses written documentation exclusively for the evaluation of research protocols. Verbal assurances or explanations are not acceptable, although PIs or their representatives may be invited to explain portions of a protocol and/or answer questions as necessary to clarify the written research protocol.

B. The JSC IRB does not duplicate the efforts of the Payload Safety Review Panel (PSRP) in its review of payload experiments equipment (Appendix E) or the efforts of SR&QA Office personnel in their review of ground-based experiments equipment. Detailed Supplementary Objectives (DSOs) and Development Test Objectives (DTOs) relating to life sciences and/or involving human interaction will be reviewed by the JSC IRB. The Board requires documented evidence of appropriate safety reviews. The particulars of each study will dictate which group reviews the research hardware.

C. No JSC IRB member may participate in the review of any research protocol in which that member has a conflicting interest, except to provide information requested by the Board. Any JSC IRB member who is a PI, Co-Investigator (Co-I), immediate supervisor or relative of the investigator(s) of a research protocol before the Board, or has any known or perceived conflict of interest, may not participate in the discussion of or vote on that protocol. A member may also abstain from voting if he or she is not technically familiar with aspects of a protocol. A simple majority vote is required for approval. Absent a consensus of the Board, each individual vote will be recorded. JSC IRB decisions will be documented in writing. The minutes will reflect the rationale for abstentions.

D. The Chairperson, or one or more experienced reviewers designated by the Chairperson from among the members of the JSC IRB, may approve human research protocols by the expedited review procedure, using the same criteria for approval as are used for non-expedited review but without the necessity for consideration by the entire JSC IRB (Appendices C and D). Only research protocol changes involving "minimal risk" or minor changes in "reasonable risk" protocols may be so approved. Approvals will be reported to the full JSC IRB at its next meeting in accordance with the current NMI.

E. The JSC IRB will be autonomous and impartial. Board members may not be added or deleted to alter Board membership for the reason of influencing a decision. Individual members must feel free to express opinions and concerns without fear of career repercussions.

F. A Secretary/Recorder and a Protocol Compliance Officer (PCO) will support the Board. The Secretary/Recorder will ensure the collection of accurate records and the publication of JSC IRB activities, including agendas, proceedings, and action items. Minutes and actions shall be published and distributed to JSC Directors, JSC IRB members, meeting attendees, and action assignees. The PCO is a medical monitor whose primary responsibility is to verify that all experiments are conducted in accordance with JSC IRB requirements. The PCO will routinely participate in tests as a monitor and representative of the JSC IRB. As such, the PCO is fully authorized to halt baseline data collection procedures in violation of JSC IRB recommendations or accepted medical practice.

1.5 Purpose of JSC IRB Review

The fundamental responsibility of the JSC IRB is to assure the health, safety, and well-being of human research subjects while ensuring ethical conduct of experimental operations. All PIs share this responsibility. The JSC IRB will review each protocol to ensure that both diagnostic and therapeutic modalities are available on spacecraft for the treatment of crew illness or injury and that the crew qualifications, training, and equipment have the concurrence of Medical Operations. The Board approves only those investigations involving "minimal" or "reasonable" risk to the human subject. In-flight animal research is of interest to the Board only in the context of crew health and safety.

1.5.1 Definitions of Risk Levels

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research protocol are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests. Examples of "Minimal Risk" activities are found in Appendix F.

Reasonable Risk: The probability and magnitude of harm or discomfort anticipated in the research protocol are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests, but these risks are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

1.6 Authority/Responsibility of the JSC IRB

1.6.1 Actions

The JSC IRB can approve, disapprove, or require changes in any research protocol submitted for review. The JSC IRB has the authority to terminate approval of research activity either not conducted in accordance with the approved research protocol or that has generated unexpected harm or excessive discomfort to a subject. In the event of a termination of approval, the JSC IRB will promptly communicate its rationale to the PI. The PI may appeal the decision by meeting with the JSC IRB or by writing the Chairperson. Experiment operations will be suspended until the appeal is resolved.

1.6.2 Sanctions for Violations

A. Any investigator may have his or her research protocol immediately suspended for non-compliance with JSC IRB recommendations in accordance with the "Common Rule" (Appendix A), for scientific misconduct, or for unethical practice. A review panel may be convened to investigate the circumstances surrounding these events.

B. The protocol may be suspended when a research subject suffers an adverse event. In this case, the JSC IRB will vote on whether or not to recommend initiating a formal investigation.

C. NASA may invoke disciplinary action against investigators whose conduct has not been in accordance with JSC IRB standards. Sanctions for noncompliance by researchers include loss of investigator privileges and funding. Sanctions may also include reprimands, and suspension or termination of employment (Appendix D).

2.0 APPLICATION: SUBMISSION OF A RESEARCH PROTOCOL[1]

2.1 Types of human research reviewed by the JSC IRB

Research reviewed by the JSC IRB can be divided into two categories:

1. Flight (human and animal) research, including KC-135 and preflight training/baseline data collection in support of flight protocols

2. Ground-based research in support of life sciences goals/objectives

2.2 Types of Research Protocols Reviewed by the JSC IRB

Research protocols reviewed by the JSC IRB are of two types:

1. Life Sciences Research Protocol: the first document reviewed by the JSC IRB. All investigators must submit this detailed, comprehensive research protocol to the JSC IRB for review. The format required by the JSC IRB is given in Appendix G.

2. Training/Baseline Data Collection Protocol: In addition to a Life Sciences Research Protocol, a detailed description of activities for a specific training session will be submitted by investigators for in-flight experiments. It will include objectives of the specific tour as well as a daily schedule of the training procedures and equipment to be used. Experience gained from training sessions and baseline data collections may result in protocol modifications. The JSC IRB therefore requires that the exact protocol for each training/baseline data collection be reviewed and approved on a tour-by-tour basis. A Training/Baseline Data Collection Protocol which contains in-flight components will be submitted for approval 6 weeks prior to crew training. Approvals for a Training/Baseline Data Collection Protocol are valid for only a 12 month period (Appendix H).

---

[1] For the purpose of this handbook, the term "research protocol" definitively means a more specific procedural document as compared with the word "proposal."

2.3 Submission Process for JSC IRB Approval

A. As a matte of general practice, all JSC human research protocols, prior to submission to the JSC IRB, will have been approved by the Scientific Merit Review Committee (SMRC) after having been submitted to and approved by one or more of the following review committees or JSC elements as appropriate:

- JSC Radiation Safety Committee
- Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee

  (For the above two committees, use forms and information provided by Appendix I as appropriate.)

- Payload Safety Review Panel (for in-flight experiments equipment)
- Safety, Reliability, and Quality Assurance Office (for ground-based experiments equipment)

B. Once approved by the SMRC and required boards, the Life Sciences Research Protocol (Appendix G) is submitted to the JSC IRB. Investigators must provide the Secretary/Recorder with 20 copies of a complete and current Life Sciences Research Protocol. When applicable, this should include pre-, in-, and postflight activities. Spacelab studies and other applicable flight studies should be routed through the designated Mission Manager or equivalent prior to JSC IRB review. Life Sciences Research Protocols for flight investigations should be submitted no later than twelve months prior to the mission for original approval. The format presented in Appendix G is to be used for ground-based investigations as well. All Life Sciences Research Protocols submitted to the Board must be signed and dated by the PI.

C. At least six weeks prior to a training session, the investigator shall provide the JSC IRB with 20 copies of the Training/Baseline Data Collection Protocol to be used (Appendix H). If applicable, the Training/Baseline Data Collection Protocol will be routed through the Mission Manager or equivalent to the JSC IRB. All Training/Baseline Data Collection Protocols submitted to the Board must be signed and dated by the PI.

D. If either the Life Sciences Research Protocol or Training/Baseline Data Collection Protocol changes, the investigator must provide details of the changes to the JSC IRB for review. The replacement pages must be dated with the changed sections indicated by bars in the margins. The replacement pages must be submitted to the Secretary/Recorder of the JSC IRB as soon as possible. The Mission Manager or equivalent must receive similar replacement pages.

E. Once the Secretary/Recorder has received a satisfactory and complete Life Sciences Research Protocol and/or subsequent Training/Baseline Data

Collection Protocols for specific tours, the investigator will be informed officially, in writing, of the meeting date at which the protocol will be reviewed. The Secretary/Recorder will check the research protocol for the SMRC letter of approval and verify that all components of the protocol have been included. Non-compliant or incomplete research protocols will be returned to the PI with the discrepancies noted. Research protocols will be distributed to Board members at least 2 weeks prior to the meeting; the agenda will be set at that time. The Board considers only written documentation for evaluation of protocols. It may be desirable to have a representative familiar with the study available to answer detailed questions or note action items from the JSC IRB.

F. No crew training or ground-based investigation will commence unless an original Life Sciences Research Protocol has received approval. All additional research protocols must be approved prior to the start of Baseline Data Collection (BDC), a training session, or KC-135 flight. Consent statements must be filed with the Secretary/Recorder of the JSC IRB and the Mission Manager or equivalent when appropriate. Responsibility for these requirements lies with the Mission Manager or equivalent, the Mission Scientist, and the PI.

2.4 Renewal of a Training/Baseline Data Collection Protocol

The PI must submit a letter to the JSC IRB 30 days prior to expiration of the 12-month approval period for a training/baseline data collection protocol stating that no changes have been made and must request a renewal of approval (Appendix J). The PI must include appropriate consent statement(s) (Appendix K). If substantive changes have been made in the research protocol, these revisions must be submitted for review at least six weeks prior to start of next training.

3.0 BOARD DECISION AND NOTIFICATION

3.1 Disposition of a Research Protocol

There are three possible dispositions of a research protocol. A simple majority vote of the membership present is required for approval. The PI will be notified in writing. A sample letter is shown in Appendix L.

A. Approval

The research protocol is acceptable as written. Any subsequent deviations or changes must be resubmitted to the JSC IRB. The PI will be informed of such approval in writing. In some cases, where minor deficiencies are found, the approval may be qualified with some stipulation that requires follow-up reports.

B. Deferred Approval

The JSC IRB did not have sufficient information to make a decision or changes are required to make the research protocol acceptable. The PI will be informed of the JSC IRB decision in writing. New information should be submitted at least

two weeks prior to the next scheduled meeting. For Training/Baseline Data Collection Protocols, it is imperative that the approval process be initiated at least six weeks before the anticipated training session.

C. Disapproval

The research protocol is not acceptable. The PI will be notified of the JSC IRB decision in writing. A decision of disapproval can not be overturned without substantial modifications to the risk-benefit aspect of the protocol. The revised protocol must be resubmitted for all required approvals.

4.0 CONDUCT OF THE RESEARCH PROTOCOL

4.1 Normal Process

A. Safe and ethical conduct of all research in conformance with JSC IRB-approved research protocols is the primary responsibility of the PI and his/her management. All research protocols must contain a section with a detailed medical monitoring plan. The plan should include provisions to pre-screen subjects when possible for hypersensitivity to any administered substances prior to experimentation. The JSC IRB will consider the adequacy of the plan. If a study requires the injection of any substance into a subject, at least one Co-I and/or another licensed physician will be present. The same applies to prescription medications administered other than by injection. Research use of Food and Drug Administration (FDA)-approved drugs for indications not in the package insert, as well as investigational new drugs, are subject to FDA restrictions. FDA Forms 1571 and 1572 are to be submitted as attachments to the Life Sciences Research Protocol (Appendix M). The JSC IRB will review all protocols for compliance with FDA requirements.

B. Members of the JSC IRB and the PCO will occasionally participate in formal, announced visits to the various facilities in which JSC IRB-approved investigations are conducted. In addition, members of the Board and the PCO may observe tests in progress on an irregular, unannounced basis to assure that the JSC IRB's recommendations are being followed. These individuals will be responsible to the Chairperson of the JSC IRB and have no relationship to the research or the researchers, e.g., no conflict of interest.

C. A medical monitor will attend ground based investigations and training sessions as deemed necessary by the JSC IRB. Qualifications and certifications required of the medical monitor shall be determined by the JSC IRB.

D. Minor equipment and procedural changes may be approved by the medical monitor during the session. Any changes that the monitor does not approve will be deferred to the full JSC IRB and that portion of the training will be delayed until the JSC IRB has ruled on the changes.

E. To ensure that no increased risk is occasioned by juxtaposed experiment research protocols, an integrated plan for pre-, in-, and postflight experiment operations must be presented to the JSC IRB for approval. This plan must include experiment requests and activities, medical operations requirements (blood/fluid) and total crew scheduling requirements for all phases of the mission.

The Mission Scientist (and/or Project Scientist) and Crew Surgeon will evaluate interactive risks to astronaut test subjects for composite experiments on each flight, including the order and sequence of experiments for each participant. A discussion of potential hazards which must be excluded or minimized includes but is not limited to interactive pharmacological risks and an assessment of potential impact of experimental medical hardware on crew performance or emergency egress. Attention should be directed toward the combined physiological or psychological impact of all procedures on the subject. The Mission Scientist and the Crew Surgeon will present the interactive profile for consideration by the JSC IRB.

This plan must be approved by the JSC IRB prior to start of training or baseline data collection. For life science intensive flights and space station missions, this approval must occur launch minus 6 (L-6) months; or L-4 months for all other missions.

F. Prior to the start of any medical study, the PI will obtain signed informed consent (either NASA/JSC Human Research Informed Consent, JSC Form 1416 or NASA/RSA Human Research Informed Consent, JSC Form 1417 (Appendix K). The PI will submit a request for human subjects (Appendix N) to the Human Test Subject Facility Recruiter.

4.2 Informed Consent

A complete description (in layman's terms) of the experiment/procedures will be included in the Life Sciences Research Protocol. A detailed description of any medical risks involved (e.g., from ionizing radiation, medications to be used, and reactions to these medications) must also be included. Experiment-peculiar interdictions or proscribed subject behavior such as exercise, dietary restrictions, medications from private physicians, and weight control medications/regimens must also be included as an attachment. This subject is addressed in Johnson Space Center Management Instruction (JMI) 7170.2 (Appendix O).

4.3 Privacy of Biomedical Research Data

A. Each investigator must submit details of a data sharing plan if applicable. A plan to protect privacy of medical data which includes safeguards for electronically stored data, should be submitted. No data attributable to an individual will be publicly released without written permission of the subject. This concept encompasses non-disclosure of an individual's name, and also requires sufficient pooling of data to preclude determining an individual's identity by combining or

cross-referencing data (e.g., height, weight, sex, and flight number may identify a specific individual).

B. The JSC IRB supports full compliance with JMI 1382.5 "Maintaining the Privacy of Biomedical Research Data" (Appendix P). This document has been modified and supplemented by "Policy Guidelines for Space Flight Medical Research Experiments", a policy approved by the Space and Life Sciences and Flight Crew Operations Directorates on March 8, 1995 (Appendix Q).

4.4 Test Readiness Review

A. A test readiness review (TRR) will be conducted prior to each "reasonable risk" test or series of tests. The review will outline the test plan, determine the readiness of the facility and test equipment, and verify the qualification certification of the test team. All test team personnel will receive a briefing detailing possible adverse reactions to the protocol and will review emergency procedures (Appendix R).

The PI will ensure that all questions are properly raised and answered. A medical monitor will attend the TRR and be informed of all procedures, reasonable risks, and all known hazards. The TRR should include all key members of the test team including those persons who will have hands-on responsibility for test operations and data collection/analysis.

B. The Test Readiness Review Board (TRRB) will sign a readiness statement to indicate approval for the test to proceed. As required, the TRRB may include representatives from SR&QA Office, Medical Monitoring, and Laboratory Support.

C. A posttest debriefing will be held with all significant test team members to discuss the test results and any test or facility anomalies

4.5 Appropriate Medical Coverage

The PI will propose the level of medical coverage for all "reasonable risk" protocols. The JSC IRB will evaluate the medical monitoring plan for each portion of the protocol. The JSC IRB typically categorizes medical coverage into four levels. Quarterly emergency drills must be conducted as part of training for those investigator teams whose protocols require Level 1 or 2 monitoring. The PI or Co-I must be physically present during performance of all protocols that require Level 1 and 2 monitoring. Responsibility for maintaining JSC crash carts and training all ancillary medical personnel in the use of equipment lies with the Medical Operations Branch. Experiments conducted during flight typically will not have equivalent monitoring due to programmatic constraints. There will be compensating real-time ground-based monitoring requirements in the case of certain flight protocols. Examples of approved medical monitoring levels for ground-based studies are found in Appendix S. A roster of JSC personnel certified in basic life support (BLS) will be maintained by the PCO.

Level 1: The Advanced Cardiac Life Support (ACLS)-certified physician must be physically present in the room at the time of the test (active monitoring). An up-to-date "crash cart" and IV pole will be collocated in the immediate vicinity of the test. Two basic life support (BLS)-certified test operators will also be present during testing.

Level 2: The ACLS-certified physician and an up-to-date "crash cart" will be immediately available in the building where the test is being conducted, within seconds of the testing area. Two BLS-certified operators will be present at all times.

Level 3: The ACLS-certified physician will be available within 15 minutes of notification.

Level 4: The ACLS-certified physician is aware of the specific testing and available for consultation.

4.6 Adverse Reactions/Anomalous Data Reporting

A. All activities will be immediately suspended if an illness or injury occurs, unless such suspension would endanger the subject. Within 24 hours of such an event the PI or Co-I must notify the Chairperson of the JSC IRB (or Alternate Chairperson), the Crew Surgeon, and the Director of SR&QA Office (Appendix D, Section 14 and Appendix T). A detailed, written report to the same person(s) should be submitted within 48 hours. Reporting of these anomalous incidents applies to training sessions as well. In addition to the above, a NASA Mishap Report (NASA Form 1627) is required (Appendix U). In-flight adverse reactions will be reported to the Crew Surgeon who will evaluate the situation and report the incident to appropriate management levels. In addition, such reactions or anomalies will be thoroughly discussed during medical postflight debriefings to determine their precise etiologies. Such incidents will include (but not be limited to):

- Adverse reactions to drugs, trauma, eye irritations, equipment failure (anomalous operation), animal bites or scratches, thrombophlebitis, burns, etc.
- Any illness or injury of a subject possibly related to the experiment.
- Any change in the environment or subject's response that could lead to some medical disturbance.
- Any substantive change from the approved research protocol.
- The subject complains of some abnormality after the protocol activity and there is reason to believe the discomfort and the protocol activity are related.

B. Any one of the following individuals has the authority to terminate the test and insist on a review of the circumstances by the JSC IRB prior to the resumption of test activities:

- Principal Investigator
- Medical Monitor, PCO, or Crew Surgeon
- Test subject
- NASA Test Director (if applicable)
- Mission Manager or equivalent
- JSC IRB Chairperson

A decision to terminate the test by any one of the above is binding upon the other responsible individuals. When a protocol has been suspended secondary to an adverse event, the JSC IRB will review the occurrence and vote on whether or not to recommend a formal investigation.

C. A database of adv[illegible] events will be maintained by the PCO and communicated to appropriate fut[illegible]vestigators, medical personnel, and subsequent subjects for similar tests. [illegible] information is protected as private medical data (Appendix P).

D. The medical aspects of a mishap involving attributable private medical data will be detailed by the Crew Surgeon/medical monitor in the medical inquiry report and will be made a part of the test subject facility medical record or the astronaut's medical record. These matters will not be included in a NASA Mishap Report (NASA Form 1627), Appendix U.

E. In conducting human research on astronauts, particularly during preflight ground-based data collection sessions, some of the data may lie outside the expected norms for the given experimental conditions of the research protocol. Procedures have been devised for the handling and reporting of such data in these cases. The steps to be followed are described in detail in Johnson Space Center Policy Directive (JPD) 7170.3 (Appendix T) and require no further elaboration.

4.7 Withdrawal of Flight Crew Subjects from Human Research

A. Given the protracted time period spent in training as subject/operator for a number of experiments (e.g., a dedicated life sciences Spacelab mission) the withdrawal of a crew member from participation in one or more experiments is a serious step which may have a cascading effect on other experiments and on the success of the mission. There are specific instances in which subjects cannot or may not withdraw from participation in human research without prejudice or penalty. In other instances, this may not be the case. These contingencies are detailed in JPD 7170.1 (Appendix V) and NMI 7100.8 (Appendix D).

B. Life Sciences and the Astronaut Office will determine by formal agreement which experiments will be treated as core experiments; withdrawal from those may lead to replacement (Appendix V). Core experiments will be indicated in the briefing before crew assignment is made.

4.8 Studies Involving Animals

A. Studies involving animals must adhere to the guidelines which are outlined in Appendices W and X. Appendix W describes animal care procedures for preflight crew training activities. Flight simulations and space flight procedures are described in Appendix X.

B. If animals are used in an experiment, the investigator must include the following information in Section 9 of the Life Sciences Research Protocol:

- Precautions to be used to maintain the NASA Flight Quality (NFQ) status and tests used to ascertain NFQ status prior to training or flight.
- Potential biohazards from all experimental animals must be assessed.

5.0 MISCELLANEOUS GUIDELINES/STANDARDS

All approved flight protocols must be implemented in accordance with NASA regulations including crew scheduling constraints.[2]

5.1 Recommended JSC IRB Electrical Standards for In-flight Instrumentation

Because of the risk from electrical hazards, the JSC IRB has set guidelines (limits) for bioinstrumentation leakage currents utilizing surface electrodes as well as for invasive instruments with regard to voltage sources or power amplifiers utilizing frequencies from direct current to 1 kHz. Electrical stimuli applied to research subjects will be evaluated for electrical safety on a case-by-case basis. Subjects instrumented with multiple bioelectric systems will be assessed in the context of possible system interactions (nominal or failure modes) such that the electrical standards are not exceeded by any interactions. Details of these electrical standards are given in Appendix Y.

5.2 Crew Venipuncture and Blood Volume Constraints

A. The following guidelines have been established to assist investigators, management personnel, and the JSC IRB in the evaluation of venipuncture and blood volume requests for a given space flight mission. The intent is to establish

[2] JSC 22359, "Crew Scheduling Constraints. Appendix K of the Space Shuttle Crew Procedures Management Plan, Revision B, January 1992".

blood volume collection and venipuncture schedules that are acceptable to Medical Operations and crew member subjects while maintaining the integrity of the investigation or mission. Investigations or missions that deviate from these guidelines will identify the specific deviation and provide appropriate supporting rationale in the required research protocol documentation.

B. If a subject has reduced iron stores at the beginning of data collection, medical therapy may correct the deficit. Crew members weighing less than 110 pounds are still eligible for blood draws because of the low volumes and prolonged time frame of the collections.

C. Medical Operations currently requires 40 cc blood draws on launch minus ten (L-10) days, L-3 days, Landing Day (R+0), and R+3 days. Data from these collections can be made available to investigators with crew member consent. Procedures for sharing information should be outlined in a data sharing plan. For a complete list of tests run, see JSC-14374, "Clinical Laboratory Support Plan for Orbital Flight Test (OFT) Missions".

D. Specific Guidelines:

- Blood draws should minimize the number of needle sticks and catheter insertions, grouping data collections as much as possible.

- If a crew member is anemic, the Crew Surgeon may cancel further blood draws, perform diagnostic tests and institute therapy.

- Total pre-, in- and postflight blood draws will not exceed 450 cc per crew member. Since this includes 160 cc of blood required by Medical Operations, 290 cc are available for other studies.

- On all space flights, in-flight draws should not exceed 50 cc per week. In-flight catheter or needle sticks should not exceed two per flight day.

- From R+7 days through R+6 months, blood draw amounts should average less than 100 cc per month.

E. Responsibilities:

- The final schedule approved by the JSC IRB will be strictly followed. The Crew Surgeon, Mission Manager or equivalent and Project Scientist will insure that the approved blood drawing protocol limits are not exceeded. The Mission Manager or equivalent and Project Scientist must report any significant discrepancy in blood draw amounts to the Crew Surgeon and the JSC IRB.

- The Crew Surgeon has the authority to cancel further blood draws for legitimate medical reasons, such as anemia or trauma. The Crew Surgeon will have the authority, in consultation with the affected crew member, to cancel further blood draws until the anemia is resolved.

- Non-astronaut studies: Total blood sample volumes will be recorded in the test subject records to ensure that participants in multiple studies do not exceed JSC IRB recommendations for total volume of blood drawn.

Note: The rationale for the above guidelines is derived from the general recommendations for blood donations. Donations are allowed only from individuals who weigh more than 110 pounds (50 kg) and who have a hematocrit greater than 35%. Every eight (8) weeks, a donation center can accept one (1) unit (400-450 cc). This schedule assumes a blood replacement rate of 10 cc per day. Autologous blood donors may give up to two (2) units per week for two to three weeks prior to elective surgery. This is based on a more realistic blood replacement rate of 50-200 cc per day, assuming adequate iron stores.

5.3 Safety Reporting Requirements for Investigations Performed at Off-site Locations

For human research investigations not conducted at JSC but involving JSC personnel as investigators or subjects, the following elements shall be included in the appropriate research protocol:

A. Detailed system description documenting all of the systems/hardware of the research/ training and their functions and relations to the research.

B. Facility information identifying all of the requirements and services that must be met or provided by the facility.

C. Hazard analysis with particular emphasis on stored energy, procedures and interfaces between the test subject and hardware, and the means by which the hazards are eliminated or controlled. The level of effort of the hazard analysis will be consistent with the hazard potential to the test subject.

D. Existing flight hazard analyses may be used for ground-based investigations provided that no differences exist between flight and ground hardware with regard to function, use, or hazards associated with the hardware.

E. Letter of "safety certification" from resident safety office or JSC IRB stating that all hardware items have been reviewed and in the opinion of the off-site safety organization are considered safe for their intended use.

Appendices

Appendices

Appendix A	Current Ethics Policies and Research Oversight Practices for Federally Sponsored Research
Appendix B	Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979
Appendix C	Section 4.7 - JSC Institutional Review Board (in: The JSC Organization JHB 1107.1)
Appendix D	Protection of Human Research Subjects (NMI 7100.8)
Appendix E	Memorandum of Understanding, JSC Institutional Review Board and JSC Payload Safety Review Panel
Appendix F	Examples of Research Activities Involving No More Than "Minimal Risk" Protocols or Previously Approved "Reasonable Risk" Protocols With Only Minor Changes
Appendix G	Life Sciences Research Protocol
Appendix H	Training/Baseline Data Collection Protocol
Appendix I	Guidelines for Radionuclide Use in Space Flight Payloads Ionizing Radiation Source Data Sheet - Space Flight Hardware and Applications (JSC Form 44) Radio Frequency/Microwave Hazard Evaluation Data (JSC Form 44A) Laser/Optical Device Hazard Evaluation Data (JSC Form 44B) Worksheet for Tissue Doses from Radiopharmaceuticals (JSC Form 44C) Worksheet for Tissue Doses from Diagnostic X-Ray Examinations (JSC Form 44D) Radiopharmaceutical Human Use Information Form (JSC Form 44E) Radiopharmaceutical Unit Dosage Receipt and Use Log (JSC Form 44F) Radiopharmaceutical Multidose Vial Preparation and Use Log (JSC Form 44G) Radioactive Material Use Authorization (JSC Form 1942) Radiation User Approval (JSC Form 1944)
Appendix J	NASA-JSC Institutional Review Board (IRB) Principal Investigator Request to Renew Approval of Human Research Protocol
Appendix K	NASA/JSC Human Research Informed Consent (JSC Form 1416) NASA/RSA Human Research Informed Consent (JSC Form 1417)
Appendix L	JSC IRB Letter of Disposition

Appendix M	FDA 1571, "Investigational New Drug Application (IND)" FDA 1572, "Statement of Investigator"
Appendix N	Request for Human Test Subject Recruiting
Appendix O	Scientific Misconduct with Regard to Human Research (JMI 7170.2)
Appendix P	Maintaining the Privacy of Biomedical Research Data (JMI 1382.5)
Appendix Q	Policy Guidelines for Space Flight Medical Research Experiments
Appendix R	Guidelines for Test Readiness Review
Appendix S	Examples of Approved Medical Monitoring Practices
Appendix T	Disposition and Reporting of Anomalous Human Research Data (JPD 7170.3)
Appendix U	NASA Mishap Report (NASA Form 1627)
Appendix V	Withdrawal of Flight Crew Subjects from Human Research (JPD 7170.1)
Appendix W	Guidelines Relative to Use of Experimental Animals During Preflight Crew Training Activities
Appendix X	Guidelines Relative to Use of Experimental Animals During Crew Training Simulations Utilizing the Flight Research Animal Holding Facility (RAHF) and General Purpose Work Station (GPWS), Chamber Simulations (Closed Environments), and Actual Space Flight
Appendix Y	IRB Guidelines Regarding In-flight Electrical Standards Associated with Bioinstrumentation to be Used for In-flight Investigative Monitoring of Shuttle Crewmembers

Appendix A

Current Ethics Policies and Research Oversight Practices for Federally Sponsored Research[1]

Introduction

In 1991, sixteen federal departments adopted a single, general set of regulatory provisions governing human subjects protections. This common federal policy, known as the "Common Rule", 45 CFR Part 46, Subpart A, specifies how research that involves human subjects is to be reviewed, the protections that such research must afford human subjects in order to be approved for funding by each signatory federal agency, and what must be included in the process of obtaining subjects' informed consent.

The Federal Policy for Human Subjects Protections (Common Rule)

The basic organizational structure for ensuring that the rights and well-being of human subjects are protected are institutional review boards (IRBs), panels often composed of physicians, scientists, administrators, and community representatives, usually at the local research institution, that review and approve any research proposal before it is submitted to a federal agency for funding. The Common Rule requires that research institutions, as a condition for receiving federal research support, form IRBs and delegate to them the authority to review, stipulate changes in, approve or disapprove, and oversee human subjects protections for all research conducted at the institution. The IRB has the authority to suspend the conduct of any research found to entail unexpected or undue risk to subjects, or that is not in conformity with the Common Rule or the institution's additional protections.

A prominent feature of the Common Rule is the requirement for the informed consent of the subject. The informed consent of a competent subject, is a cornerstone of modern research ethics. Ideally, informed consent should be viewed as an ongoing process of communication between researcher and the subjects of their research. The required elements of informed consent as enumerated in the Common Rule are summarized as follows:

- a statement that the study involves research, an explanation of the purposes of the research, and a description of the procedures to be followed;
- a description of any reasonably foreseeable risks or discomforts to the subject;
- a description of any benefits to the subjects or to others that might reasonably be expected;
- a disclosure of alternative procedures or courses of treatment;

[1] Excerpts taken from: Final Report - Advisory Committee on Human Radiation Experiments, October 1995, Chapter 14, Part III, pp. 675-693 (Pittsburgh:US Government Printing Office).

- a statement describing the extent to which confidentiality of records identifying the subject will be maintained;

- for research involving more than minimal risk, an explanation of the availability and nature of any compensation or medical treatment if injury occurs;

- identification of whom to contact for further information about the research and about subjects' rights, and whom to contact in the event of a research-related injury;

- a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time.

Research Involving Ionizing Radiation

Beyond the strictures of the Common Rule, research involving either external radiation or radioactive drugs usually undergoes additional review for safety and risk (including a review of radiation dose) prior to IRB review at the local research institution. Most medical institutions have a radiation safety committee (RSC) responsible for evaluating the risks of medical activities, whether for diagnostic, treatment, or research purposes and limiting the exposure of both employees and subjects to radiation. In addition, research and medical institutions that perform basic research involving human subjects and radioactive drugs must have such studies reviewed and approved by a radioactive drug research committee (RDRC) -- a local institutional committee approved by the Food and Drug Administration (FDA) to ensure that safeguards, including limitations on radiation dose, in the use of such drugs are met. Notwithstanding the prior review and approval of either or both of these radiation committees, the IRB must also assess the risks and potential benefits of the proposed research before approving it.

Scope of Programs of Research Involving Human Subjects at NASA

Both intramurally and extramurally, NASA conducts ground-based and in-flight biomedical research involving human subjects related to space life. In fiscal year 1994 NASA spent approximately $25 million on ground-based human subjects research.

Administrative Structures and Procedures for Research Oversight

Some (federal) departments audit or review IRB performance routinely while others conduct investigations only when problems emerge. The method, intensity and frequency of research oversight and inspection activities is a direct function of the level of staffing and budgetary resources.

The IRB is an administrative unit that must itself comply with certain requirements of the Common Rule in terms of its composition, review procedures, and substantive review criteria; it must also direct researchers to

comply with other requirements of the rule, such as adequate informed consent and fair subject selection procedures.

Effectiveness of IRBs

The success or failure of the federal regulations governing human subjects research depends on the effectiveness of IRB's in carrying out their responsibilities: assessing research proposals prior to their funding, stipulating any changes in the research protocol or informed consent procedure that strengthen the protections afforded the subjects, disapproving inadequate or excessively risky research proposals, reviewing ongoing research at least every twelve months to ascertain that the research poses no undue risks to subjects, and taking action quickly to correct any failing in safeguarding subjects' rights and welfare.

Federal agencies overseeing human subjects research conducted in-house or supported extramurally establish a structure whereby research proposals involving human subjects are peer reviewed for scientific merit as well as for IRB approval and the adequacy of subject protections, negotiate assurances with research institutions that ensure that adequate protections will be in place for research subjects, verify that institutions, their IRBs, and researchers are complying with the federal human subjects regulations, and investigate complaints of noncompliance and adverse outcome for subjects of research.

Principal investigators are required to report any adverse outcomes to the IRB and the IRB must have procedures to ensure that the appropriate institutional officials and the funding agency are informed as well. The method, intensity and frequency of research oversight and inspection activities is a direct function of the level of an agency's staffing and budgetary resources.

Sanctions for Violation of Human Subjects Protections

Withdrawal of assurance and, with that action, of research funding; suspension or termination of IRB approval of research; and disciplinary action against agency employees engaged in human subjects research are the sanctions available under the Common Rule. The Common Rule authorizes IRBs to suspend or terminate their approval or research that is not conducted according to the IRB's requirements or when a research subject suffers an adverse event in the course of participation that requires investigation.

Federal agencies may also take disciplinary action against employees involved in human subjects research for failure to follow human subjects protection rules. Sanctions for noncompliance by intramural researchers include loss of investigator privileges. Sanctions may also include reprimands, suspension, or termination of employment.

HISTORY OF THE COMMON RULE

1947	The Nuremberg Code
1953	NIH Clinical Center Policy *In addition to a statement of principles similar to the Nuremberg Code, this policy required prior review of research involving healthy volunteers and patients that would be exposed to hazardous research procedures by an independent, local group of researchers.*
1962	Kefauver-Harris amendments to the Food, Drug and Cosmetic Act *Required the informed consent of subjects participating in drug research.*
1964	Declaration of Helsinki
1965	National Advisory Health Council resolution requires prior review and protection for informed consent.
1966	PHS-wide policy for the protection of human subjects in extramural clinical research, Policy and Procedure Order No. 129 (PPO # 129) *Required that an awardee institution, through a committee of institutional associates, review proposed research in terms of protections afforded the rights and welfare of subjects, informed consent, and its risks and potential medical benefits.*
1967	PPO # 129 expanded to include intramural research and contracts.
1971	PHS policy extended to all human subjects research conducted or supported by HEW, published as the "Institutional Guide to DHEW Policy on Protection of Human Subjects". *Required documentation of the informed consent process and the signature of the research subject or the subject's representative.*
1974	Title II of the National Research Act (P.L. 93-348) *Required codification of DHEW policy in regulations, imposed a moratorium on federally funded fetal research, and established requirements for IRB review of all human subjects research at any institution receiving DHEW funding.*

	DHEW regulations for the protection of human research subjects. 45 C.F.R. 46 *Established IRB review procedures in accordance with Title II. Later in the same year DHEW published regulations providing additional protection for pregnant women and fetuses.*
1974-1978	National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research *Issued reports and recommendations on fetal research; on research involving prisoners, psychosurgery, children, and the mentally infirm; on IRBs and informed consent; and, in* The Belmont Report, *discussed criteria for distinguishing research from the practice of medicine and ethical principles underlying the protection of subjects.*
1978	Revised DHEW regulations governing protections for pregnant women, fetuses, and in vitro fertilization (subpart B of 45 C.F.R. 46), and prisoners (subpart C) published
1980-1983	President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research *Charged with, among other responsibilities, reviewing federal policies governing human subjects research and determining how well those policies were being carried out. Recommended that all federal agencies adopt the DHHS regulations for the protection of human subjects (1981).*
1981	DHHS published a revision of 45 C.F.R. 46, responding to recommendations of the National Commission *The revision set out in greater specificity IRB responsibilities and the procedures IRBs were to follow.* FDA regulations at 21 C.F.R. 50, governing informed consent procedures, and at 21 C.F.R. 56, governing IRBs, revised to correspond to DHHS regulations to the extent allowed by FDA's statute
1982	President's Science Advisor, Office of Science and Technology Policy (OSTP), appointed an interagency committee to develop a common federal policy for the protection of human research subjects.
1983	DHHS regulation governing protections afforded children in research (subpart D of 45 C.F.R. 46) published

1986	Proposed common federal policy for the protection of human research subjects published
1991	Final common federal policy published on June 18, codified in the regulations of fifteen federal agencies and adopted by the CIA under executive order *This common policy, known as "the Common Rule," is identical to the basic DHHS policy for the protection of research subjects, 45 C.F.R. 46, subpart A. Other sections of the DHHS regulation provide additional protections for pregnant women, fetuses, in vitro fertilization (subpart B), prisoners (subpart C), and children (subpart D). Several agencies have adopted these additional provisions as administrative guidelines. The FDA made conforming changes in its informed consent and IRB regulations.*

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Office of the Secretary
Protection of Human Subjects

Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979[1]

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk/benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

---

[1] Reprinted from U.S. Government Printing Office: 1988-201-778/80319; GPO 887-809

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
Dorothy I. Height, President, National Council of Negro Women, Inc.
Albert R. Jonsen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.
Pat[illegible] King, J.D., Associate Professor of Law, Georgetown University Law Center.
Ka[illegible]ebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.
*Dav[illegible] W. Louisell, J.D., Professor of Law, University of California at Berkeley.
Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.
Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.
*Robert H. Turtle, LL.B., Attorney, VomBaur, Coburn, Simmons & Turtle, Washington, D.C.

* Deceased.

Table of Contents

Belmont Report

Ethical Principles and Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This code became the

prototype of many later codes[2] intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted .

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals.[3] By contrast, the

---

[2] Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

[3] Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even

term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.[4]

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence, and justice.

1. Respect for Persons. - Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from

---

when a procedure applied in practice may be ... the other person, it remains an intervention designed to enhance the well-being of a particular individual ... groups of individuals; thus, it is practice and need not be reviewed as research.

[4] Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. *Beneficence.* - Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children - even when individual research subjects are not direct beneficiaries. Research also makes is possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice. - Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a

particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent. - Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their

care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence - especially where possible sanctions are involved - urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. *Assessment of Risks and Benefits.* - The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons.

The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm,

physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from resear-

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject - or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the

nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. - Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition. [FR Doc. 79-12065 Filed 4-17-79; 8:45 am]

4.7 JSC Institutional Review Board

4.7.1 Purpose

To establish the JSC Institutional Review Board (IRB) and to delegate authority to approve the conduct of human research and recommend expedited review(s) of human research protocols to the Director, Space and Life Sciences.

4.7.2 Applicability

JSC: The policy set forth applies to JSC and will be followed by all members of investigative teams in all research experiments involving human test subjects which are funded or sponsored by JSC; conducted in spacecraft, JSC facilities or aircraft; or which involve JSC to any degree.

Cooperative Arrangement or Agreement: All human research conducted under a cooperative or reimbursable arrangement or agreement entered into by JSC and another Government agency, private entity, non-Federal public entity, or foreign entity must also comply with the terms and conditions of this document and NMI 7100.8.

4.7.3 Establishment

The JSC IRB is established by the Center Director in accordance with NMI 7100.8, "Protection of Human Research Subjects." The JSC IRB will review all ground-based and aeronautical flight research involving human subjects that is conducted at JSC, or extramural research in which JSC personnel and/or facilities are involved. Additionally, all research involving human subjects, including flight crews, performed in NASA spacecraft will be reviewed by the JSC IRB.

4.7.4 Membership

The minimum membership of the JSC IRB is:

Chairperson	Senior Medical Officer of the Space and Life Sciences Directorate (S&LSD)
Member	Alternate Chairperson (Executive Secretary)
Member	A life scientist appointed by the Chairperson
Member	A flight surgeon
Member	A representative from the Legal Office
Member	A representative from the Safety, Reliability, and Quality Assurance Office
Member	An astronaut
Member	A non-life-sciences employee
Member	A non-NASA, full-time Federal employee

Members of the JSC IRB are appointed by the Center Director and are Federal employees. Members are expected to attend regularly. At least one third of the membership will be physicians. Up to three ad hoc members in specialized disciplines may be added to the JSC IRB on a temporary, non-voting basis as deemed appropriate

by the Chairperson. The member position filled by a non-life-sciences employee will be rotated among the Center directorates and offices.

The permanent Chairperson will periodically designate an alternate Chairperson to afford experience in conducting the meetings while the former will retain overall control of the standing JSC IRB.

All members of the JSC IRB are voting members. The Chairperson will vote only in the event of a tie. A majority of the JSC IRB members present is required to evaluate and approve a protocol and must include the Chairperson (or alternate Chairperson) and representatives of the Astronaut Office (a representative from the Astronaut Office is required for evaluation of flight studies), SR&QA Office, and Medical Operations. Every member is required to vote on each issue except in conflict of interest cases or when lack of technical familiarity with aspects of a protocol would impede the decision process. If there is no consensus of the Board, the vote of each member will be recorded and the reason for a negative vote or abstention will be stated.

4.7.5 Authority

The JSC IRB has the authority to approve, disapprove, or require changes in the proposed human research protocols and procedures covered by NMI 7100.8.

The JSC IRB may conditionally approve a protocol or recommend changes to disapproved protocols which may result in their approval. The JSC IRB has the authority to suspend or terminate its approval of research activities that are not being conducted in accordance with approved protocol or the policies set forth in NMI 7100.8 or that have been associated with unexpected serious harm to subjects.

4.7.6 Responsibility

The fundamental responsibility of the JSC IRB is to assure the health, safety and well-being of human research subjects while ensuring ethical conduct of experimental operations.

4.7.7 Functions

The JSC IRB will provide advice and counsel to the Authorized JSC Official on matters within the scope of this document and as required by referenced management instructions, including but not limited to:

- Review of all NASA ground-based or aeronautical flight and all space-flight proposed human research protocols submitted to the Authorized JSC Official prior to funding, approval, or execution;

- Review of all flight payloads experiments or procedures involving humans as test subjects, ensuring that protocols and safety procedures conform to NASA policy;

- Issue guidelines to be followed in the conduct of all human research measurements and experimental procedures, flight and ground-based;

- Maintain documentation of JSC IRB activities as prescribed in NMI 7100.8.

4.7.8 Reporting

The Chairperson and members of the JSC IRB report to the Center Director for all matters involving the Board.

4.7.9 Meetings

Meetings will be convened by the Chairperson of the JSC IRB on a routine basis or when a request is made by the Authorized JSC Official, Program Director, JSC Center Director, or a test subject to evaluate a human research experiment which may affect the health or well-being of any human subject.

4.7.10 Records and Staff Supporting Services

A secretary-recorder will ensure accurate recording and publication of JSC IRB activities, including agendas, proceedings, and action items. Minutes and actions shall be published and distributed to JSC Directors, JSC IRB members, meeting attendees, and action assignees.

The Chairperson will appoint a Protocol Compliance Officer (PCO) to verify that all experiments are conducted in accordance with JSC IRB requirements. The PCO will report any protocol violation immediately to the Chairperson.

The Scientific Merit Review Committee must approve all JSC human research protocols prior to submission to the JSC IRB. All protocols will have been submitted to and approved by one or more of the following review boards or JSC elements as appropriate:

- JSC Radiation Safety Committee
- Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee
- Payload Safety Review Panel (reviews equipment for in-flight experiments)
- Safety, Reliability, and Quality Assurance (reviews equipment for ground-based experiments)

The Legal Office will provide assistance with the Informed Consent Statements.

4.7.11 Subcommittees

The Chairperson, or one or more experienced reviewers designated by the Chairperson from among the members of the JSC IRB, may approve human research protocols by the expedited review procedure, using the same criteria for approval as is used for non-expedited review but without the necessity for consideration by the entire JSC IRB. Expedited review can only take place for low hazard or "minimal risk" protocols or previously approved protocols with minor changes. Such reviews shall be communicated to the JSC IRB by the Chairperson at the next meeting of the full JSC IRB.

4.7.12 Conflicts of Interest

No JSC IRB member may participate in the review of any research protocol in which that member has a conflicting interest, except to provide information requested by the Board. Any JSC IRB member who is a Principal Investigator, Co-Investigator, immediate supervisor or relative of the investigator(s) of a research protocol before the Board, or has any known or perceived conflict of interest, may not participate in the discussion of or vote on that protocol.

4.7.13 Duration

The JSC IRB will remain in effect until dissolved by the Center Director.

4.7.14 References

a. NMI 7100.8, "Protection of Human Research Subjects."

b. NMI 8900.1, "Medical Operations Responsibilities for Manned Space Flight Programs."

c. JSC-20483B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

Change 1 to:
JPG 1107.1A, The JSC Organization
Section 4, Committees, Boards, and Panels
Part 4.7, JSC Institutional Review Board

Approved:

Original signed by:
H. David Short

H. David Short
Director, Space and Life Sciences

Original signed by:
George W. S. Abbey

George W. S. Abbey
Director, Johnson Space Center

NASA
MANAGEMENT
INSTRUCTION

NMI 7100.8B
Effective Date: August 8, 1995
Expiration Date: August 8, 1999

Responsible Office: U/Office of Life and Microgravity Sciences and Applications

Subject: PROTECTION OF HUMAN RESEARCH SUBJECTS

1. PURPOSE

This Instruction sets forth NASA policies and procedures for the protection of human research subjects.

*2. APPLICABILITY AND SCOPE

a. This Instruction follows the provisions of NASA regulations contained in 14 CFR Part 1230 and 45 CFR Part 46, "Protection of Human Subjects," promulgated by the Office of Science and Technology Policy.

b. This Instruction applies to NASA Headquarters and NASA Centers and will be followed by all members of the research team in all research experiments involving human subjects which are funded or sponsored by NASA, conducted in NASA facilities, aircraft, or spacecraft, or which involve NASA to any degree. All human research conducted under a cooperative or reimbursable arrangement or agreement entered into by NASA and another Government agency, private entity, non-Federal public entity, or foreign entity must also comply with the terms and conditions of this Instruction.

c. Research activities that are exempted from this Instruction are those in which the involvement of human subjects is limited solely to the use of survey or interview procedures unless (1) the information obtained is recorded in such a manner that human subjects are identified directly or can be identified indirectly through designators or through identifiers linked to the subjects, and (2) any disclosure of the human subjects' responses outside the research that could reasonably place the subjects at risk for criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. Also exempt is research involving the collection or study of existing data, documents, records, pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded by the Principal Investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.

*3. AUTHORITIES

a. The National Aeronautics and Space Act of 1958, as amended, 42 U.S.C. 2451 et seq.

b. "Protection of Human Subjects," 14 CFR Part 1230 and 45 CFR Part 46.

4. DEFINITIONS

For the purposes of this Instruction; the following definitions apply:

*a. Minimal risk means that the proposed research does not add greater harm or discomfort, considering probability and magnitude, than that encountered in the daily lives of healthy individuals.

b. An Institutional Review Board (IRB) is a committee approved by NASA and established, in accordance with paragraph 5 of this Instruction or approved by the Department of Health and Human Services (DHHS) under a current Multiple Project Assurance (MPA), to review human research proposals and activities for the adequacy of procedures that protect human subjects in research.

*c. Research is a systematic investigation, including development, testing, and evaluation, designed to test a hypothesis, enable conclusions to be drawn, and thereby develop or contribute to general knowledge. Research is described in a formal protocol that sets forth an objective and a set of procedures designed to reach the stated objective.

d. Funded pertains to research that is partially or completely paid for by NASA.

*e. Sponsored research is not funded by NASA but is approved by NASA to utilize NASA, other Government, or foreign facilities, equipment, or personnel, including space vehicles.

*f. Human subject means a living person other than the Principal Investigator who is an integral part of a test, or other substantive evaluative procedure and about whom the Principal Investigator (whether professional or student) obtains (1) research data through intervention or interaction, or (2) identifiable private information. Intervention includes both physical-testing procedures by which data are collected (for example, equipment, articles, or other substances inserted in, applied to, or otherwise used on that person) and manipulation of the subject or the subject's environment for research purposes. Interaction includes communication or interpersonal contact between the investigator and the subject. Private information includes information provided for specific purposes and about behavior which the individual can reasonably expect that no observation or recording is taking place and which the individual can reasonably expect will not be made public.

*g. Principal Investigator means a researcher who has overall responsibility for all aspects of the funded and/or sponsored research project.

*h. Authorized NASA Official is the Associate Administrator for Life and Microgravity Sciences and Applications, NASA Headquarters, who is empowered, subject to conditions and limitations imposed by immediate superiors, to authorize human research. However, when the official is also acting as a Principal Investigator for a particular proposed investigation, authorization will be requested from the immediate superior. All or part of the authority may be redelegated, without power of further redelegation, to one of the following positions:

(1) A senior Headquarters NASA employee, normally the Deputy Associate Administrator, who reports to the Authorized NASA official; or

(2) The NASA Center Director(s).

The Authorized NASA Official(s) shall ensure that the Administrator and the Chief Medical Officer, Office of Space Flight, Associate Administrator for the office sponsoring the research, and the Associate Administrator for Safety and Mission Assurance are kept fully and currently informed, through official channels, of significant actions, problems, or other matters of substance related to the exercise of this authority.

*i. Crewmember is an astronaut or a payload specialist or aviation personnel assigned to a spacecraft or an aircraft mission.

*j. Life sciences research includes biomedical, biological, human factors / psychological, environmental health, and life-support experimentation.

*k. Serious harm means temporary illness or injury or permanent disability.

5. NASA IRB'S

a. The NASA Center Directors will establish an IRB to review all ground-based and aeronautical flight research involving human subjects that is participated in or conducted at their Center or, by prior arrangement, have another NASA IRB review the research proposals.

b. All research involving human subjects, including flight crews, performed in NASA spacecraft will be reviewed by the IRB at the Johnson Space Center (JSC).

*6. NASA IRB AUTHORITY RESPONSIBILITY AND FUNCTIONS

a. Authority

(1) The IRB has authority to approve, disapprove, or require changes in the proposed human research protocols and procedures covered by this Instruction.

A decision of "disapproved" cannot be overturned, but a decision of "approved" may be changed to "disapproved" by an Authorized NASA Official.

(2) The IRB may conditionally approve a protocol or recommend changes to disapproved protocols which might result in their approval. The IRB has the authority to suspend or terminate its approval of research activities that are not being conducted in accordance with the approved protocol or the policies set forth in this Instruction or that have been associated with unexpected serious harm to subjects. Any suspension or termination of approval will include a statement of the reasons for the IRB's action and will be promptly reported to the Principal Investigator, the NASA Center Director, and the Authorized NASA Official. If an IRB disapproves, suspends, terminates, or conditionally approves a research activity, the Principal Investigator will be given the opportunity to appeal the decision by meeting with the IRB or through written correspondence with the Chairperson of the IRB.

b. IRB Responsibility. The primary responsibility of the IRB is to protect the rights and ensure the safety of every person who is a subject of any research in NASA facilities, including NASA aircraft or spacecraft, or is a subject of NASA-funded or NASA-sponsored research.

c. IRB Functions

(1) Reviews all NASA ground-based or aeronautical flight and all space-flight-proposed human research (the latter applies to JSC's IRB only) prior to funding, approval, or execution. Except when an expedited review procedure is used, this review of proposed research will be held only at convened meetings at which a majority of the members of the IRB are present. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.

(2) Conducts a continuing review of human research covered by this Instruction at intervals appropriate to the degree of risk but not less than once per year, including the review of implementation of

informed consent and success of safety precautions taken to date, and to determine whether or not proper information was given to the subject during the process.

(3) Defines for each approved experiment the extent to which the actual consent process and/or the conduct of the research will be monitored. If monitoring is deemed necessary, this may be accomplished by appointment of a monitor with specified responsibilities or direct monitoring by the IRB.

(4) Maintains documentation of IRB activities as prescribed in paragraph 9 of this Instruction.

7. IRB MEMBERSHIP

*a. Each IRB will have at least five members who shall regularly attend meetings. The IRB shall consist of persons with varying backgrounds and sufficient knowledge of the experimental environment and conditions to promote complete and adequate review of research activities conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, including consideration of race, gender, ethnic, and cultural background and sensitivities to such issues as community attitudes to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The NASA Center Director will appoint the members of the IRB and select a full-time, senior level NASA employee as the Chairperson. The members must have the competence required to review the human research activities covered by this Instruction and to determine the acceptability of the proposed research relative to applicable laws, safety regulations, health standards, and ethical codes. One of the members will be designated as the Executive Secretary.

*b. The IRB shall include culturally diverse members not entirely of one gender or race including a (1) NASA-employed physician, member of the Chief Counsel's Office, and member of the Center's Safety Office; (2) at least one additional member whose expertise is in a nonscientific area such as medical ethics; (3) at least one member cognizant of the operational aspects of aerospace environment; and (4) at least one additional member who is not otherwise affiliated with NASA and who is not a part of the immediate family of a person affiliated with NASA.

c. No IRB member may participate in the review of any proposal in which that member has a conflicting interest, except to provide information requested by the IRB.

d. The IRB may invite experts to help review special or difficult issues which require competence beyond or in addition to that available on the IRB. These persons may not vote with the IRB.

*e. The Executive Secretary appointed by the Chairperson of the IRB will chair the IRB in the absence of the Chairperson.

* 8. IRB CONVENING AUTHORITY

Meetings shall be convened by the Chairperson of the IRB on a routine basis or when a request is made by the Authorized NASA Official, program director, a NASA Center Director, or a test subject to evaluate a human research experiment which may affect the health or well-being of any human subject.

9. IRB RECORDS

a. The IRB shall prepare and maintain adequate documentation of IRB activities including the following:

(1) Copies of all research proposals reviewed; scientific evaluations, if any, that accompany the proposals approved; sample consent documents; progress reports submitted by Principal Investigators; and reports of injuries to subjects.

(2) Minutes of IRB meetings, which will be in sufficient detail to indicate attendance at the meetings; actions taken by the IRB; the vote on these actions, including the number voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

*(3) Records of continuing review and monitoring activities.

(4) Copies of all correspondence between the IRB and the investigators.

*(5) A list of IRB members identified by name, earned degrees, representative capacity, indications of capabilities such as board certification and licenses, and any employment or other relationship between each member and NASA. A copy of this list and changes thereto will be sent to the Authorized NASA Official.

(6) Written procedures for the IRB.

(7) Statements of significant new findings provided to subjects, as required by paragraph 10e (5) of this Instruction.

*(8) Written procedures for assuring prompt reporting to the IRB and the Authorized NASA Official of any unanticipated problems involving risks to subjects, others, serious noncompliance with this policy or the Principal Investigator's protocol, requirements of the IRB, and suspension or termination of IRB approval.

*(9) A summary of IRB activities based on the minutes.

*b. The records required by this Instruction shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be entered into a secure computerized data base, under the management of the Executive Secretary of the IRB, and accessible for inspection and copying by authorized representatives of NASA at reasonable times and in a reasonable manner. Handling of the information contained in the records and the computerized data base is subject to the appropriate guidelines and policies.

*10. INFORMED CONSENT

a. Except as provided in subparagraph f, no Principal Investigator may involve a human being as a subject in research covered by this Instruction unless the Principal Investigator has obtained the informed consent of the subject or the subject's legally authorized representative. Such consent shall be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative will be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights or which releases or appears to release the Principal Investigator, the sponsor, the institution, or its agents from liability for negligence.

b. For basic elements of informed consent, except as provided in subparagraph e in seeking informed consent, the following information shall be provided to each subject:

(1) A statement that explains that the study involves research. It should also include an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

(2) A description of any reasonably foreseeable risks or discomforts to the subject.

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(5) A statement describing the extent, if any, to which confidentiality of records, identifying the subjects, shall be maintained. Special attention should be given to explaining the unique problem of confidentiality with electronically stored data bases.

(6) For research involving more than minimal risk, an explanation as to whether any compensation and medical treatments are available if injury occurs, and, if so, of what they consist and any other relevant information.

(7) An explanation of whom to contact for answers to pertinent questions about the research and the research subject's rights and whom to contact in the event of a research-related injury to the subject.

(8) Except as provided in subparagraph d, a statement that participation is voluntary, refusal to participate shall involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If the subject, in fact, cannot withdraw at any time (because unwise, dangerous, or impossible), the circumstances must be explained to the subject in writing in the informed consent document.

(9) Subjects concerned about protocol violations may request a meeting with the relevant IRB.

c. Consideration for withdrawal from nonspace-based research includes the following:

(1) Research subjects can withdraw from participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(2) In the event that a subject withdraws from non-space flight human research, NASA reserves the right to replace that individual with another test subject.

d. Consideration for withdrawal from space-based research includes the following:

(1) Research subjects may withdraw from participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(2) In the event that the test subject is a crewmember and

(a) the IRB-approved life science experiment is part of the central or core function of the mission,

(b) the crewmember was clearly and completely informed of the experiment prior to assignment to the mission,

(c) the crewmember formally consented to participate in the experiment,

(d) no substantial change has occurred in the protocol since the crewmember's consent, and

(e) no new scientific information has surfaced indicating that the initial protocol presents a more than minimal increase in health or safety risk, withdrawal from research may result in replacement of that individual from that mission. This action shall be based on the determination that it is in the best interest of the Government.

(3) The determination of whether all conditions in subparagraph d(2) have been met shall rest with the IRB that approved the initial protocol. In the case of NASA astronauts or international mission specialists, final determination and disposition shall rest with the Associate Administrator for Space Flight in consultation with the mission-sponsoring organization. For payload specialists, final disposition shall rest with the Associate Administrator for Life and Microgravity Sciences and Applications, with the concurrence of the Associate Administrator for Space Flight.

(4) When a crew member has withdrawn and all conditions in subparagraph d(2) have been met, withdrawal will not influence career opportunities; however, it could result in prejudice regarding assignments to a mission in which similar life-science experiments are central or core to the mission.

e. Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) which are currently unforeseeable.

(2) Anticipated circumstances under which the subject's participation may be terminated by the Principal Investigator without regard to the subject's consent.

(3) Any additional costs to the subject that may result from participation in the research.

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

(5) A statement that the subject will be informed of significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation.

(6) The approximate number of subjects involved in the study.

*(7) Any collective impact of multiple protocols, if applicable.

f. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this Instruction or may waive the requirements to obtain informed consent, provided that the IRB finds and documents the following:

(1) The research involves no more than minimal risk to the subjects.

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects.

(3) The research could not practicably be carried out without the waiver or alteration.

(4) Whenever appropriate, the subjects shall be provided with additional pertinent information after participation.

g. The informed consent requirements in this Instruction are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

h. Nothing in this Instruction is intended to limit the authority of a physician to provide emergency medical care to the extent that the physician is permitted to do so under applicable Federal, State, or local law.

11. DOCUMENTATION OF INFORMED CONSENT

a. Informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

b. The consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by paragraph 10 of this Instruction. This form may be read to the subject or the subject's legally authorized representative, but, in any event, the Principal Investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.

(2) A "short form" written consent document, stating that the elements of informed consent required by paragraph 10 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the "short form" itself is to be signed by the subject or the representative. However, the witness shall sign both the "short form" and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the "short form."

12. CRITERIA FOR IRB APPROVAL OF HUMAN RESEARCH

a. The following requirements must be satisfied for the IRB to approve the human research covered by this Instruction:

*(1) Risk to subjects are minimized (a) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (b) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes, taking into account the collective impact of multiple protocols.

*(2) Risk to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits, taking into account the collective impact of multiple protocols, that may result from the research (as distinguished from risks and benefits of therapies that subjects would

receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) The voluntary informed consent of each prospective subject or the subject's legally authorized representative shall be obtained. In addition, this consent shall be documented. The human research consent form shall be written to contain at least all elements listed in paragraph 10b (and 10e, if appropriate). Not all risks are readily identifiable, and the research subject should be so informed.

(4) Proof that the subject or the subject's beneficiaries will be compensated by means of insurance, worker's compensation, or the like in the event that the subject suffers illness, disease, injury, loss, or death as a result of the human research must accompany the proposal. Lack of such information shall serve as a basis for disapproval of the proposed research.

(5) Where applicable, the research proposal shall contain provisions for monitoring the data collected to ensure the safety of the subjects. Other information that should be part of a human research proposal is listed in attachment A.

*(6) Safeguards shall be provided to protect the privacy of subjects and the confidentiality of data, especially electronically stored data. Biomedical data, if retrievable by personal identifier, is subject to the Privacy Act and is maintained under the NASA System of Records, NASA 10 HERD, Human Experimental and Research Data Records.

(7) Protocols shall be submitted and approved prior to the participation of any human subject in any portion of the experiment.

*(8) Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted. In the case of space flight, considerations should be given to the habitability conditions and the level of medical care available in the event of illness or injury.

13. EXPEDITED REVIEW

*a. In the case of human research of the type listed in attachment B, the IRB may conduct an expedited review which shall consist of a review by the Chairperson, or one or more experienced reviewers designated by the Chairperson from among the members of the IRB, using the same criteria for approval as is used for any non-expedited review but without the necessity for consideration by the entire IRB. The IRB may also use the expedited procedure to review minor changes in previously approved research during the period for which approval is authorized.

b. In conducting an expedited review, the reviewer(s) shall exercise all of the authorities of the IRB, except that the reviewer(s) may not disapprove the research. A research activity may be disapproved only after review in accordance with the nonexpedited procedure described in this Instruction. A reviewer may recommend that the proposal receive a full review by the IRB if the reviewer determines that the research involves more than minimal risk.

c. The reviewer(s) who approves research proposals using the expedited review procedure, shall either directly or through the Chairperson report to the IRB on such approvals at the next meeting of the IRB.

14. REPORTS OF INJURIES, ILLNESS, OR DISEASE

*a. The Principal Investigator shall immediately suspend the human research (unless such suspension would endanger the human subject) and inform the IRB Chairperson, and appropriate investigations shall be initiated in the event of the following:

(1) Any unexpected injury, illness, or disease incurred by the subject as an apparent result of the human research.

(2) Any change in the experimental environment or in the subject's response that could lead to medical problems.

b. Occurrence of any instance requiring medical attention is to be noted in the subject's medical records or made available to the subject's physician. Once a human research experiment is suspended, IRB review and approval is required before the experimentation proceeds.

*c. All such events shall be reported immediately to the IRB, and additionally to NASA, e.g., to the NASA Center Safety Officer; the Authorized NASA Official; and the Chief Medical Officer, Office of Space Flight, NASA Headquarters; the Office for Protection from Research Risks (OPRR), National Institutes of Health, if the institution conducting the research holds an OPRR approved MPA.

15. PROTOCOL MODIFICATIONS

*a. The protocol cannot be modified unless a formal request with appropriate justification is approved by the IRB or the reviewer (in the case of an originally expedited review). If the reviewer or the IRB determines that the modification increases the risk(s) to the subject, it shall require the execution of a new human research consent form.

b. For space flight experiments, it is recognized that a human research protocol may need to be modified in flight, as procedures are refined to comply with operational constraints. Substantive changes to human research protocols, which become necessary during flight, shall require the approval of a majority of a quorum of the IRB. The Chairperson or designee shall expeditiously seek this approval in a meeting or by telephone contact with members of the IRB. The Mission Operations Control Room Surgeon must be immediately told of this requested substantive change and has the authority to temporarily suspend the experiment until the IRB can review the request.

*16. ASSURANCES FROM PARTICIPATING INSTITUTION

a. All institutions proposing human research that is funded by NASA shall give written institutional assurance, as provided in 14 CFR 1230.103, to the Authorized NASA Official. An MPA on file with OPRR shall satisfy this requirement. In the case of foreign institutions, assurances must include that their research proposal has been approved by an IRB, meeting at least the standards of the Declaration of Helsinki.

b. Assurances for projects utilizing NASA facilities, equipment, or personnel will not be accepted. NASA IRB review and approval will be required.

c. NASA Centers shall file MPA's with the Authorized NASA Official.

d. MPA's and Single Project Assurances will use the model form of the DHHS.

e. MPA's will be issued for a term of not more than 5 years.

17. SANCTIONS

a. Any NASA Principal Investigator involved in human research, who does not comply with the policies and procedures of this Instruction or does not comply with the protocol as approved, may have his or her research immediately suspended or terminated when such noncompliance becomes known to the appropriate IRB, NASA Center Director, or Center Director of Life Sciences. Such noncompliance may be cause for sanctions ranging from reprimand to revocation of funding.

b. Principal Investigators not employed by NASA, who are responsible for human research that is funded or sponsored by NASA or is performed in NASA facilities, aircraft, or spacecraft and who do not comply with the general guidelines described in this Instruction or do not comply with the protocol as approved, may have their research immediately suspended or terminated and shall also be subject to appropriate sanctions.

*c. The Associate Administrator for Life and Microgravity Sciences and Applications may convene a NASA Headquarters review panel to investigate the circumstances surrounding all cases of noncompliance. The review panel shall be chaired by a designated senior Headquarters official who has no apparent or appearance of conflict of interest. The membership shall consist, as a minimum, of a representative from the Office of the General Counsel, a representative from the Aerospace Medicine Occupational Health Advisory Subcommittee, a representative from the Office of Safety and Mission Assurance, and a representative from the Aerospace Medicine and Occupational Health Division, Office of Life and Microgravity Sciences and Applications, NASA Headquarters. After review of the circumstances, the Associate Administrator for Life and Microgravity Sciences and Applications, in consultation with the General Counsel, will recommend appropriate action to the NASA Administrator who has the final authority to prescribe sanctions and to publicize these sanctions.

18. CANCELLATION

NMI 7100.8A, dated November 18, 1986.

Original Signature:
Daniel S. Goldin
Administrator

ATTACHMENTS:
A. Partial Contents of a NASA Human Research Proposal.
B. Research Activities Which May Be Reviewed Through Expedited Review Procedures.

DISTRIBUTION:
SDL 1

August 8, 1995

ATTACHMENT A
NMI 7100.8B

PARTIAL CONTENTS OF A NASA HUMAN RESEARCH PROPOSAL

The following information will be included with the proposal upon submission for peer review:

1. Name of the organization conducting the research or for which the research is being conducted.

2. Name and qualifications of persons who will conduct the human research.

*3. An explanation of the reason that the use of human subjects is required and a plan ensuring equitable selection of research subjects with particular reference to race and gender.

4. Possible inconveniences, discomforts, illnesses, diseases pain, and risks to the subject.

5. A description of the hazard controls and safety precautions to be applied.

6. Expected duration of the study, which will include approximate beginning and ending dates.

7. The extent of any physical examinations to be given by medical personnel is as follows:

   a. Initially, to ascertain that the subject's health status has been adequately established to certify that the subject is capable of undertaking the research.

   b. During the course of the research.

   c. At the completion of the research.

8. Wage, salary, or other payment, if any, to be paid to the subject for participating in the research.

9. Source (Federal or state compensation acts and insurance) and general description (include example of dollar amounts) of compensation, if any, to be received by a subject or the subject's legally authorized representative in the event of injury or death. Assistance in the preparation of this information may be obtained from the appropriate NASA Center Chief Counsel's Office, or if the subject is or will be a Government employee, the NASA Center Personnel Office.

10. Availability of medical personnel, if applicable, and an adequate medical facility within a reasonable distance to the location where research is performed.

* Changed by this revision.

Indicate whether a physician will be present at all times or on call; if on call, the physician's location during the performance of the research.

11. Information concerning the human research that is intended to be communicated to the subject during the course of obtaining the subject's consent.

*12. The human research consent form, including the provision that subjects concerned about protocol violations may request a meeting with the relevant IRB.

13. Evidence of review and approval by the sponsoring organization's IRB.

*14. A plan for ensuring privacy and protecting the confidentiality of data with particular attention to an electronic data base.

August 8, 1995

ATTACHMENT B
NMI 7100.8B

RESEARCH ACTIVITIES WHICH MAY BE REVIEWED THROUGH EXPEDITED REVIEW PROCEDURES

*Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the following categories (carried out through standard methods) may be reviewed by the IRB through the expedited review procedure authorized in 45 CFR 46.110 and 14 CFR 1230.110.

1. Collection of hair and nail clippings, in a nondisfiguring manner, deciduous teeth, and permanent teeth if patient care indicates a need for extraction.

2. Collection of excreta and external secretions, including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labor.

*3. Recording of data from subjects 18 years of age or older, using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (e.g., X-rays, microwaves, ultraviolet light, and bright lights).

4. Collection of both supra- and subgingival dental plaque and calculus, provided that the procedure is not more invasive than routine prophylactic scaling of the teeth and that the process is accomplished in accordance with accepted prophylactic techniques.

5. Voice recordings made for research purposes such as investigations of speech defects.

6. Moderate exercise by healthy volunteers.

7. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

8. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the Principal Investigator does not manipulate the subject's behavior and the research shall not involve stress to the subjects.

* Changed by this revision.

Memorandum of Understanding
JSC Institutional Review Board
and
JSC Payload Safety Review Panel

Purpose

To define and clarify the joint responsibilities of JSC Institutional Review Board (IRB) and JSC Payload Safety Review Panel (PSRP) in reviewing NASA-sponsored experiments involving human research subjects. The IRB shall combine their biomedical expertise with the technical expertise and engineering capability of the PSRP in an effort to ensure that NASA-sponsored experiments involving human research subjects (i.e., human physiology experiments) are safe.

Roles and Responsibilities

1. The role of the physicians, human physiologists, and other professional support personnel of the IRB in ensuring the safety of human test subjects for in-flight and NASA-sponsored ground-based experiments is as follows:

    a. The IRB shall review, from a biomedical perspective, all human research protocols for potential hazards and hazard controls with respect to all in-flight and NASA-sponsored ground-based experiments. The IRB will ensure that all credible hazards are identified and are adequately controlled. Potential hazards and their controls to be addressed by the IRB include excessive electrical shock, ultrasound, personal fatigue, adverse effects of drugs or injectable solutions, excessive collection of blood, or other single or combined physiological stress factors.

    b. The IRB or their appointed representative shall establish safe physiological limits for intentionally applied electrical, ultrasound, laser, and other types of electromagnetic impulses to the various parts of the body, as required for a given experiment system.

    c. The IRB shall be responsible for ensuring the safety of all equipment used in human in-flight research. In this context, the IRB shall rely on the PSRP to review the design and operation of <u>all</u> custom-made equipment and modifications of off-the-shelf devices that could be hazardous to the in-flight test subjects or nearby participants in an experiment.

    d. The IRB or their designees shall be responsible for ensuring that a planned sequence of human experiments does not create excessive fatigue or other adverse effects on the test subjects.

    e. The IRB shall ensure that all ground-based human research (experiment) hardware shall be found safe for use in its surroundings by Health, Safety, and Environmental Compliance (HSEC) Office (NA3).

2. The role of the engineers and other support persons on the PSRP in this joint responsibility to ensure crew safety is as follows:

   a. The PSRP shall review the design and operation of payload experiment hardware for its compliance with the safety requirements in NSTS 1700.7B, "Safety Policy and Requirements for Payloads Using the Space Transportation System," or in the NSTS 1700.7B, ISS Addendum, "Safety Policy and Requirements for Payloads Using the International Space Station." The PSRP will ensure that all identified hazards are adequately controlled, and that these controls have been adequately verified.

   b. The PSRP shall forward to the IRB for their resolution any potential hazard identified at a payload safety review that requires the biomedical expertise of the IRB to determine its risk potential. This will help the PSRP confirm that controls for this hazard are adequate.

   c. The PSRP shall send to the IRB requests for the establishment of physiological limits for ultrasound, electrical shock, and other physiological stresses that could result from either planned use or a malfunction during use of the equipment. These physiological limits will be used by the PSRP in determining whether the design and controls on the equipment items under review are adequate.

To facilitate the flow of information between the IRB and the PSRP, a representative of the Space and Life Sciences Directorate will be a member of both groups. This individual shall attend safety reviews of flight experiments involving human test subjects conducted by both groups. This person will also keep each group informed of the deliberations and actions of the other group regarding human research experiments of common interest to both groups.

Original Signature:
Harold F. Battaglia, 5-31-96
Harold F. Battaglia/MA2
Manager for Payload Safety

Original Signature:
Lawrence F. Dietlein, M.D., 5-31-96
Lawrence F. Dietlein, M.D./SA
Chair, JSC IRB

INFORMATIONAL NOTE:
The other system safety groups that review experiments with human test subjects from an engineering perspective include the: Safety and Mission Assurance Review Team (SMART), mail codes NS2 and SM2; Safety, Reliability, and Quality Assurance (SR&QA) Office IRB Working Group, mail codes NA3 and NS2; Health, Safety, and Environmental Compliance Officer (HSEC), mail code NA3; and the Payload and Crew Equipment Assurance Branch, mail code NS2. The SMART reviews all U.S. experiment hardware to be transferred to the Mir; the SR&QA Office IRB Working Group reviews all experiment protocols submitted to the JSC IRB; the HSEC reviews all NASA-sponsored ground experiments and equipment; and the Payload and Crew Equipment Assurance Branch reviews all EVA and related flight payload experiments, detailed supplementary objectives (DSOs), developmental test objectives (DTOs) and risk mitigation experiments not reviewed by the PSRP.

Examples of Research Activities Involving No More Than "Minimal Risk" Protocols or Previously Approved "Reasonable Risk" Protocols With Only Minor Changes

(1) Collection of hair and nail clippings, in a non-disfiguring manner; deciduous teeth, and permanent teeth if patient care indicates a need for extraction.

(2) Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labor.

(3) Recording of data from subjects 18 years of age or older using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject, or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echosonography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (for example, x-rays, microwaves).

(4) Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an 8-week period and no more than two venipunctures per week, from subjects 18 years of age or older and who are in good health and not pregnant.

(5) Collection of both supra- and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth, and the process is accomplished in accordance with accepted prophylactic techniques.

(6) Voice recordings made for research purposes such as investigations of speech defects.

(7) Moderate exercise by healthy volunteers.

(8) The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

(9) Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subjects' behavior and the research will not involve stress to subjects.

(10) Research on drugs or devices for which an investigational exemption is not required.

Lyndon B. Johnson Space Center
Institutional Review Board
LIFE SCIENCES RESEARCH PROTOCOL

The Lyndon B. Johnson Space Center (JSC) Institutional Review Board (IRB) reviews both ground-based and space flight-related human research protocols. Life sciences protocols using human test subjects must be approved by the JSC IRB when research is conducted in spacecraft, JSC facilities, JSC aircraft, or at other centers or institutions when JSC civil service or contractor personnel are directly involved in the research activities. In addition, all research protocols involving space flight crews must be approved by the JSC IRB. Only complete protocols will be reviewed by the JSC IRB. Verbal agreements are not satisfactory and all protocols must be presented to the JSC IRB in writing. Refer to JSC 20483B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations" for additional information.

GENERAL INFORMATION

- The format described here is to be used by investigators preparing the documentation required by the JSC IRB for protocol review. It is important to be thorough and detailed. Do not eliminate anything. Prepare the package in the order presented below. Incomplete protocols WILL be returned.

- A completed, signed PROTOCOL COMPLETION CHECKLIST (Section 18.0) must be submitted with the protocol.

- The Principal Investigator must forward 20 copies of the signed LIFE SCIENCES RESEARCH PROTOCOL to the secretary/recorder of the JSC IRB if the protocol requires full JSC IRB review. Forward 3 copies of the signed Life Science Research Protocol if the protocol will be reviewed by the expedited review process.

- Deadline for submitting a protocol:

  FLIGHT STUDIES

  Full Committee Review: One year prior to mission.

  Expedited Review (minimal risk protocols and previously approved reasonable risk protocols with only minor changes): These protocols may be submitted at any time. If you have questions whether a protocol qualifies for expedited review or not, please contact Dr. Lawrence Dietlein, JSC IRB Chairperson, (713) 483-6291.

  GROUND-BASED STUDIES

  Full Committee Review: Should be submitted 6-12 months before intended start date for review by the JSC Scientific Merit Review Committee (SMRC) and JSC IRB, which

occurs before formal peer review by Headquarters. However, proposals in response to NASA Research Announcements (NRAs), Announcement of Opportunity (AO), etc. must follow the schedule imposed by Headquarters and the announced JSC IRB review schedule.

Expedited Review (minimal risk protocols and previously approved reasonable risk protocols with only minor changes): These protocols may be submitted at any time. If you have questions whether a protocol qualifies for expedited review or not, please contact Dr. Lawrence Dietlein, JSC IRB Chairperson, (713) 483-6291.

- If you require assistance with the completion of the protocol, or have questions regarding the process, please contact Ms. Mary Flores, the JSC IRB secretary/recorder, at (713) 212-1468. The JSC IRB Chairperson and the Alternate Chairperson are also available to assist you.

- "NASA/JSC Human Research Informed Consent", JSC Form 1416, and "NASA/RSA Human Research Informed Consent", JSC Form 1417 are available on the Internet by typing "http:/stic.jsc.nasa.gov/" (without quotes), then selecting option number 7.

LIFE SCIENCES RESEARCH PROTOCOL FORMAT

The format below is to be used during the preparation of the protocol. Deviation from this format will result in the protocol being returned to the Principal Investigator. Number each section as shown.

1.0 COVER PAGE

Each protocol is to have a cover page which contains the following information:

1.1 Spacelab or Shuttle Flight Designation (if applicable)

1.2 Experiment Designation

1.3 Functional Objective Designation(s)

1.4 Title of Project

1.5 Organization Conducting the Research

A. Name the organization conducting the research or for which the research is being conducted. Normally it is the institution with which the Principal Investigator (PI) is affiliated.

B. Research protocols submitted by JSC civil service investigators must include the signature of the authorizing NASA official (Branch or Division Chief).

1.6 Investigators

A. List all investigators starting with the PI. Include each individual's position and affiliation, mailing address, telephone and fax numbers, and e-mail address if available. Attach a curriculum vitae for each investigator as an appendix at the end of the protocol. *The PI must sign the cover page.*

B. List technical personnel who will aid in and/or conduct the research. Attach qualifications as an appendix at the end of the protocol. The JSC IRB is interested in the qualifications of the technical staff that will be interacting with the test subjects, because they will be operating equipment or performing procedures on them.

2.0 TABLE OF CONTENTS

All protocols must include a Table of Contents which divides the protocol into major sections identical with those presented in this guideline. Appendices should be numbered or lettered sequentially.

3.0 ABSTRACT

Briefly describe the purpose, general implementation plan, and expected results. This description of the overall project should be a stand alone summary and should not be more than half a page (500 words).

4.0 HYPOTHESIS(ES)

The hypothesis(es) should be clearly and succinctly stated. The JSC IRB must consider scientific merit as a factor in weighing risk vs. benefits. This summary should abstract the details to be included in the Section 5 below.

5.0 PURPOSE OF RESEARCH

This section may be handled by attachment (as an appendix) of information submitted in the original proposal. However, the investigator should ensure that the following information is included:

Background and Significance - Discuss briefly the development of key factors or principles which led to the formulation of hypothesis. Reference to pertinent scientific literature is essential.[1] Provide an account of the preliminary studies by the principal investigator or other associated personnel that are pertinent to the proposed study. References and titles of appropriate related publications should be included; reprints (no more than five) may be attached to the protocol.

---

[1] Not required for a Detailed Supplementary Objective (DSO).

New Information Expected - Explain the results that may be expected and their relevance to the aforementioned overall goals of the project.

6.0 STATISTICAL ANALYSIS

Describe how the data will be analyzed. Indicate the statistical methods to be used, power of the statistical method, number of subjects required, etc.

7.0 RATIONALE FOR USE OF HUMAN SUBJECTS

Explain why humans are a necessary part of the study. Include a plan for ensuring equitable selection of research subjects with particular reference to race and gender.

8.0 RESEARCH PLAN AND SCHEDULE

FLIGHT STUDIES

Give an overview of what will be accomplished during preflight training/baseline data collection sessions, in-flight experimentation, and postflight data acquisitions. For example, familiarization with the concepts of the experiment, procedures to be learned, equipment to be used, data collection, etc.

Dates/Duration - Give the expected duration of the study, which will include approximate beginning and ending dates. Provide as close an approximation as possible. Detailed schedules for Spacelab investigations should be included in the Training Protocol.

Place(s) of Training/Test/Baseline Data Collection - List the location(s) where data collection will be performed.

Subjects - Provide flight personnel designation, e.g., Mission Specialist (MS) MS1, MS2, MS3, Payload Specialist (PS) PS1, PS2, PS Backup, Commander (CDR), and Pilot (PLT).

GROUND-BASED STUDIES

State the overall general goals of the project; list specific and realistic objectives the proposed research is intended to accomplish. The relevance of the objectives to the overall goal must be clearly stated.

Study Schedule - Provide an estimate of the study duration, and a tentative start date. Present a timetable that reflects the progression of the study phases described above, including the dates of the testing. State all important milestones for the conduct of the study.

Facilities and Performance Site - Describe all the facilities in which the study will be conducted including any training facilities that will be used.

Management Plan - Clearly identify the roles of each of the investigators in reference to the conduct of the study. Include any laboratory or medical support staff required and their responsibilities.

Consultants & Collaborators - Succinctly describe the expertise of consultants and/or collaborators and their responsibilities in the study. Attach a letter of confirmation from each member stating his/her consent to participate in the project, and in the specified capacity or role.

ALL STUDIES

Data Privacy/Confidentiality - Briefly describe the procedures which you will employ to maintain confidentiality of subject identity and results. Include a plan for ensuring the privacy and protecting the confidentiality of data as required by JMI 1382.5, with particular attention to electronic databases. Indicate where the information is to be stored, the type of format to be used to store the information, and most importantly, who will have access to the information and under what circumstances. The investigator should also develop a plan for the ultimate long-term archiving at JSC of both raw and reduced data.

Data Sharing - Data and/or specimens may be shared among investigators as specified in each investigator's initial protocol. Identify other investigators with whom you wish to share data/samples. If appropriate, a table summarizing venipuncture and blood volume limits for the investigation should be provided. Values should be consistent with the guidelines in JSC 20538, Revision B.

Anomalous Data/Adverse Reactions Reporting - Include a statement indicating familiarity with Johnson Space Center Policy Directive 7170.3, "Disposition and Reporting of Anomalous Human Research Data." Outline a plan for reporting anomalous data/adverse reactions.

Injury/Illness Reporting Plan - Include a plan for reporting any illness or injury of a subject possibly related to the experiment.

9.0 EXPERIMENTAL PROTOCOLS AND EQUIPMENT

This section contains some of the most important information used by the JSC IRB. It is from this section that the JSC IRB may identify potential problems that might be overlooked by the investigators. Experience has shown that incompleteness of this section is one of the major reasons for JSC IRB non-approval.

FLIGHT STUDIES

Preflight Training and Baseline Data Collection - Describe preflight training and baseline data collection in terms of step-by-step procedures and equipment used. All equipment must be identified. In those instances where any hardware is used for training or ground-based testing, the PI is responsible for providing detailed descriptions and hazard analyses as an attachment to the protocol. The PI is also responsible for maintaining configuration control of the hardware to prevent any modifications that would compromise the hazard

analyses. Inspection records must be provided to assure the hardware configuration and to assure adherence t test requirements and procedures. Functional test and check-out of equipment utilizing non-flight crew personnel is required. All equipment, whether commercial, modified commercial, or custom designed, used for fit and functional testing, must be inspected by the Safety, Reliability, and Quality Assurance (SR&QA) Office. These results, together with equipment safety certification, must be submitted by the PI to the JSC IRB prior to flight crew usage.

In-Flight Activities - List step-by-step procedures and equipment used, approximate duration of the testing, how many crew subjects are necessary, and how many times the experiment will be performed.

Postflight Activities - If postflight testing of flight personnel is necessary, note how many times the test will be done, when, where, and what procedures and equipment will be used.

GROUND-BASED STUDIES

Outline all the details of the experiment design and procedures to be used to accomplish the specific aims of the project. If the study involves more than one phase, or multiple protocols, summarize the interrelation of these component parts here. The description of the design and methods should include the following:

Protocol Design - Describe details of all the methods, materials, and procedures to be employed in the study and their sequencing and frequency. If new methodologies are proposed, clearly describe them and justify their need by discussing their advantages over currently approved/accepted ones.

Samples - Describe all methods of sample collection, processing, and disposal of biological samples with particular attention to the handling of radioactive and other hazardous materials.

Equipment - List all the required hardware for conducting the experiment and processing the samples. Include separate lists of ground-based equipment and flight hardware.

10.0 HAZARD ANALYSES AND SAFETY PRECAUTIONS

FLIGHT STUDIES

- Detail the conceivable hazards that might be encountered during the study and the precautions that will be taken to avoid them. The sample analysis form (Attachment 1) may be used if desired. For research involving animal handling, list precautions employed for minimizing zoonoses.

- Include a statement in the protocol such as: "All experiments are to be tested if possible on non-flight-crew personnel prior to each mission".

- If animals are used in an experiment, the protocol MUST include:
  - Precautions to be used to maintain the NASA Flight Quality (NFQ) status and tests used to ascertain NFQ status prior to training or flight.
  - Potential biohazards from all experimental animals must be assessed.

- Below is the format to be used when preparing the hazard analysis/safety plan:

A. PREFLIGHT ACTIVITIES

POTENTIAL (proximate and remote) HAZARDS - For <u>each</u> potential hazard provide the following information:

a. POTENTIAL HAZARD CAUSE
b. EFFECTS OF THE HAZARD
c. ASSESSMENT: SEVERITY & PROBABILITY
   Severity categories: Reasonable/Minimal
   Probability categories: High/Medium/Low/Extremely Low
d. PROTECTION TO MINIMIZE RISKS
   Include level of medical coverage required during experiment activities

B. IN-FLIGHT ACTIVITIES

POTENTIAL (proximate and remote) HAZARDS - For <u>each</u> potential hazard provide the following information:

a. POTENTIAL HAZARD CAUSE
b. EFFECTS OF THE HAZARD
c. ASSESSMENT: SEVERITY & PROBABILITY
   Severity categories: Reasonable/Minimal
   Probability categories: High/Medium/Low/Extremely Low
d. PROTECTION TO MINIMIZE RISKS
   Include level of medical coverage required during experiment activities

C. POSTFLIGHT ACTIVITIES

POTENTIAL (proximate and remote) HAZARDS - For <u>each</u> potential hazard provide the following information:

a. POTENTIAL HAZARD CAUSE
b. EFFECTS OF THE HAZARD
c. ASSESSMENT: SEVERITY & PROBABILITY
   Severity categories: Reasonable/Minimal
   Probability categories: High/Medium/Low/Extremely Low
d. PROTECTION TO MINIMIZE RISKS
   Include level of medical coverage required during experiment activities

<u>GROUND-BASED STUDIES</u>

Medical Safety Risks and Hazards - Describe all anticipated hazards from the procedures (especially biological sample collections, new diagnostic procedures and treatments), materials (radioactive substances, etc.), or any other experiment-related conditions, including immediate, delayed, or long-term effects. Include assessment of degree of risk (minimum, reasonable, or high) and proposed acceptable risk-benefit ratio. Make sure to include assessment of residual risk.

Medical Safety Precautions - Describe details of medical intervention procedures in the event of an adverse reaction. Include information on the availability of a physician and medical facilities during and after the study, and post-experiment medical check up requirements, and precautionary measures to avoid any complications (immediate and delayed) that are experiment related.

ALL STUDIES

If radioactive materials are administered to subjects in the study, provide evidence of approval by the JSC Radiation Safety Committee. While the same protocol can be undergoing simultaneous review by both committees, final approval from the JSC IRB will be withheld until evidence of approval by the JSC Radiation Safety Committee has been received.

11.0 POSSIBLE INCONVENIENCES OR DISCOMFORTS TO SUBJECTS

List additional factors that do not fall into the category of hazards, but that should be considered.

12.0 EXTENT OF PHYSICAL EXAMINATIONS

FLIGHT STUDIES

In many cases, reliance on the annual physical examination for flight personnel is all that need be stated. Include a statement that subjects are flight personnel and their annual physical will be relied upon. If a special physical examination or special test is required, describe it and state why it is needed.

GROUND-BASED STUDIES

Indicate the extent of any physical examinations to be given by medical personnel as follows:

- Initially, to ascertain that the subject's health status has been adequately established to certify that the subject is capable of undertaking the research.
- During the course of the research
- At the completion of the research

13.0 AVAILABILITY OF A PHYSICIAN AND MEDICAL FACILITIES

FLIGHT STUDIES

State if a flight surgeon and/or medical facilities will be required preflight, in-flight, or postflight.

GROUND-BASED STUDIES

Indicate whether a physician or medical monitor will be present at all times or on call; if on call, state the physician's location during the performance of the research. Include the qualifications/certification required of the physician/medical monitor.

ALL STUDIES

This section should include provisions to pre-screen subjects when possible for hypersensitivity to any administered substances prior to experimentation.

14.0 INFORMED CONSENT

The Principal Investigator has the difficult task of explaining the proposed activity to a potential subject in enough detail and in appropriate language so as to assure that the potential subject fully understands what he/she is consenting to and that the consent is based on complete knowledge or the nature and risk of the procedure.

The JSC Institutional Review Board has the equally difficult task of determining whether or not the consent procedure proposed by the Principal Investigator adequately assures legally informed consent by the subject. The Principal Investigator should consider the following when preparing subject consent:

- Include information concerning human research to be communicated to the subjects in the course of obtaining their informed consent. Along with a *signed NASA/JSC or NASA/RSA Human Research Informed Consent statement, attach a summary, signed by the subject, describing in layman's terms the procedures the subject will undergo.* The detailed summary of the research procedures must specifically list the risks associated with the procedures to be employed, the possible adverse reactions of all medications to be administered, and the risks/hazards resulting from exposure to ionizing radiation. Further, the investigator must clearly specify all forms of subject behavior interdicted by the research protocol (exercise, diet, medications, etc.).

- The subject will be free to withdraw from the research at any time. (Describe any circumstances under which it would be hazardous or unwise to do so).

- The identity of human subjects will not be released to the general public without his or her consent unless specifically required by law.

- There will be no additional wage, salary, or other remuneration of any form paid, given, or in any manner delivered to the test subjects of this investigation where the subjects are National Aeronautics and Space Administration (NASA) employees or NASA contractor employees, and the terms of the contractors with NASA provided for participation as subjects in approved experiments.

- The human research subjects are NASA employees, NASA contractor employees or independent contractors, and the training/testing is part of their employment or contractual circumstances. Therefore, NASA is responsible for compensation for injury,

death, or property damage to the extent required by the Federal Employees Compensation Act or the Federal Tort Claims Act.

- If applicable, include the following statement in the consent, "Since the KC-135 is considered to be a public aircraft within the meaning of the Federal Aviation Act of 1958, as amended, and as such does not hold a current airworthiness certificate issued by the Federal Aviation Administration, any individual manifested to board the KC-135 should determine before boarding whether his/her personal life or accident insurance provides coverage under such conditions."

- The following clause is required if the study involves the use of a drug or device that is still under an investigational new drug (IND) number or investigational device exemption (IDE) number and the records may therefore require inspection by the Food and Drug Administration.

  "I have a right to privacy, a[illegible] all information that is obtained in connection with this study and that can be identi[illegible] with me will remain confidential as far as possible within state and federal law. Info[illegible]tion gained from this study that can identify me will be released to no one othe[illegible]han the investigators, my physician, (insert name of pharmaceutical or medical device company) and the United States Food and Drug Administration, which, through its regulatory powers, may inspect records involving research participants. The results of this study may be published in scientific journals without identifying me by name."

- Include the provision that subjects concerned about protocol violations may request a meeting with the relevant IRB.

- The subject consent form must identify the activity to be conducted, name(s) and the phone number of the individual(s) who are to conduct the activity and state the purpose of the activity. It must describe any procedures which are deemed to be experimental in nature and indicate the risks attendant thereto. It must also refer to any prior experience gained in human use or state that no prior human use has occurred and indicate the experience which has been acquired in animal studies.

- A statement should be made about expected or potential reactions resulting from all procedures to be performed that are not deemed to be experimental. The benefits, if any, that could accrue from the activity should be described and a statement made as to whether the benefit would accrue to the individual subject or to society in general. Alternative procedures that could be used in lieu of the experimental procedures must be described. An offer to answer any inquiries concerning the procedure should be made in writing. The subject should also be informed in writing that he/she may discontinue participation in the activity at any time without prejudice to the subject.

- If personal data are to be acquired from surveys, questionna[illegible]s, or medical records it is necessary to inform the subject of the criteria used by which [illegible]e or she was selected to be a subject. Describe the purpose for which the data are being collected, indicate any benefits to be gained by the subject's participation in the activity, and state what risks (physical, psychological, or social) or possible detrimental effects that may accrue to the subject.

- When the activity proposes to use normal subjects, the subject should be informed that no benefit will be derived from his/her participation. The inducements offered to a normal subject should be consistent with the degree of remuneration and shall not unduly influence the subject to participate in the activity.

- If randomization (by chance) is used to select a subject population, the subject must be so informed. If a placebo (inactive agent) is involved, the subject must also be informed that he/she may receive the experimental modality or a placebo (inactive agent). The consequences of placebo therapy must be explained.

- The investigator should incorporate into the subject consent the length of time required for participation in the activity (whether this is continuous or intermittent), any requirement for follow-up examinations or studies, and whether or not there will be limitations or constraints on the physical activities of the subject after the activity is completed.

- If monitoring procedures are required during the activity, the type, number and frequency of such procedures should be explained and the risks or discomforts of each should be described. If the performance of such procedures will incur additional expense to the subject, he/she should be so informed.

- If the research subject or his/her insurance company will be expected to pay for any expenses incurred by participation in the research protocol, this must be explained in the consent form.

REGARDLESS OF THE TYPE OF STUDY, THE INFORMED CONSENT PROCESS SHOULD INCLUDE THE FOLLOWING:

Subject Briefing. Describe all the necessary information concerning the study that will be explained to the subjects at the briefing session. Include a list of personnel that will attend the briefing and the procedures that will be explained or demonstrated at the briefing.

Subject Information Handout. Attach a handout to the consent form that clearly states in simple language all the procedures employed in the study, hazards and risks involved, safety precautions during and after the study, benefits and coverage, subjects' rights and remuneration, and any post-experiment instructions.

Consent Forms. Include the appropriate JSC Form 1416 or 1417 required by the JSC Institutional Review Board that is duly filled with information regarding the study and the investigator. The subject information handout (B, above) must be attached to the consent form.

Each subject must be given a copy of the consent statement he or she has signed as well as any attachments thereto.

15.0 RESEARCH PERFORMED AT OFF-SITE LOCATIONS

For human research investigations not conducted at JSC but involving JSC personnel as investigators or subjects, the following elements shall be included in the appropriate research protocol:

A. Detailed system description documenting all of the systems/hardware of the research/ training and their functions and relations to the research.

B. Facility information identifying all of the requirements and services that must be met or provided by the facility.

C. Hazard analysis with particular emphasis on stored energy, procedures and interfaces between the test subject and hardware, and the means by which the hazards are eliminated or controlled. The level of effort of the hazard analysis will be consistent with the hazard potential to the test subject.

D. Existing flight hazard analyses may be used for ground-based investigations provided that no differences exist between flight and ground hardware with regard to function, use, or hazards associated with the hardware.

E. Letter of "safety certification" from resident safety office or JSC IRB stating that all hardware items have been reviewed and in the opinion of the off-site safety organization are considered safe for their intended use.

16.0 OTHER FUNDING SOURCES

Include a statement regarding any funding source (other than NASA) supporting this research, e.g., NIH, or NSF. Attach a copy of the Single Project Assurance or Multiple Project Assurance, as appropriate.

17.0 ADDITIONAL ATTACHMENTS TO LIFE SCIENCES RESEARCH PROTOCOL

- Approval letter from the PI's Institutional Review Board (Human Research or Ethics Committee)
- Approval letter from the Scientific Merit Review Committee (SMRC)
- A copy of the Institutional Safety Authority's most recent certification of all related equipment
- Research use of drugs for indications not in the package insert is subject to Food & Drug Administration (FDA) restrictions. FDA forms 1571, "Investigational New Drug Application (IND)" and FDA 1572 "Statement of Investigator" are to be submitted as attachments to the Life Sciences Research Protocol.

- If applicable, approval from one of more of the following committees:

  - JSC Radiation Safety Committee
  - Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee
  - Payload Safety Review Panel
  - Safety, Reliability, & Quality Assurance

- If external radiation sources or radionuclides are employed at JSC, their use must have the approval of the JSC Radiation Safety Committee. Attach a copy of JSC Form 1942 or JSC Form 1944. In addition, the following forms must be completed as appropriate: JSC Forms 44, 44a, 44b, 44c, 44d, 44e, 44f, and 44g.

18.0 PROTOCOL COMPLETION CHECKLIST

It is the responsibility of the PI to verify that all required information has been included in the protocol. A checklist has been developed to help eliminate possible confusion regarding the content of a protocol (Attachment 2). Protocols will not be accepted by the JSC IRB without a completed, signed checklist.

ANALYSIS OF POTENTIAL HAZARDS

TITLE: _____ PAGE_____OF_____

RESPONSIBLE PERSON(S) _____ DATE_____

NO.	POTENTIAL HAZARD	CAUSE	EFFECT	ASSESSMENT SEV: REAS/MIN PRB: H/M/L/EL	PROTECTION TO MINIMIZE RISKS

PROTOCOL COMPLETION CHECKLIST

Section	Page Number (write N/A if not applicable)
1.0 COVER PAGE (signed by PI)	
Curriculum vitae(s)	
Qualifications for Technical Personnel	
2.0 TABLE OF CONTENTS	
3.0 ABSTRACT	
3.0 HYPOTHESIS(ES)	
5.0 PURPOSE OF RESEARCH	
Copies of Reprints/Supporting Information	
6.0 STATISTICAL ANALYSIS	
7.0 RATIONALE FOR USE OF HUMAN SUBJECTS	
8.0 RESEARCH PLAN AND SCHEDULE	
Expected Study Duration & Location	
Conformation Letter from Consultants/Collaborators	
Protection Plan for Personal and Medical Data	
Data Sharing Plan	
Venipuncture Plan (pre, in-, and post)	
Anomalous Data/Adverse Reaction Reporting Plan	
Injury/illness Reporting Procedures	
9.0 EXPERIMENTAL PROTOCOLS AND EQUIPMENT	
Hardware Description/Hazard Analysis	
Protocols and procedures	
Flight Training Protocols	
Flight Crew Procedures	
10.0 HAZARD ANALYSIS/SAFETY PRECAUTIONS	
Description of All Medical Risks	
11.0 POSSIBLE INCONVENIENCES OR DISCOMFORTS TO SUBJECTS	
12.0 EXTENT OF PHYSICAL EXAMINATIONS	
13.0 AVAILABILITY OF A PHYSICIAN AND MEDICAL FACILITIES	
Medical Monitoring Plan	
14.0 INFORMED CONSENT	
Human Research Informed Consent	
Summary of Risk in Layman's Terms	
Statement of Insurance for Subjects	
Subject withdrawal policy	
Subject payment and source of funds	
15.0 RESEARCH PERFORMED AT OFF-SITE LOCATIONS	
16.0 ADDITIONAL ATTACHMENTS TO LIFE SCIENCES RESEARCH PROTOCOL	
IRB Approval from PI's Institution	
Institutional Safety Authority Certification	
Other JSC Committee Reviews and Approvals	
FDA Forms	
17.0 OTHER FUNDING SOURCES	
Copy of SPA or MPA Sent to NIH (if required)	
18.0 PROTOCOL COMPLETION CHECKLIST (signed by PI)	

Signature of Principal Investigator: _____

Training/Baseline Data Collection Protocol[†]

Spacelab Designation _____

Experiment # _____

Training Session # _____

Location of Training _____

Dates of Training _____

Subjects _____

1. Title

2. Organization Conducting the Research

3. Investigators and Technical Personnel

List the name of the Principal Investigator (PI), address, and phone number. Reference to the Life Sciences Research Protocol may be made for other investigators and technical personnel. If changes have been made, note the changes and supply qualifications if not already on file.

4. Objectives of This Tour

Stating the objectives of the specific training session will aid those who are conducting the tour to focus on what they wish to accomplish and help the JSC Institutional Review Board (IRB) to understand the intent of an individual training session. Relate the objectives to the results of previous training sessions (if any).

5. Detailed Daily Schedule of Training Activities

The schedule will provide the JSC IRB an idea of the intensity and duration of each day of training as well as the step-by-step procedures and equipment to be employed. Reference can be made to the Life Sciences Research Protocol for details, but each step must be listed and any deviation from the Life Sciences Research Protocol must be noted. If substantive or permanent changes from the Life Sciences Research Protocol have been made, supply dated and marked replacement pages for the Life Sciences Research Protocol.

6. Hazards

Restate all of the potential hazards for the specific training session as extracted from the Life Sciences Research Protocol.

[†] All headings in BOLD are to be included in the protocol in the order listed.

7. Informed Consent Form

If required, attach the appropriate consent form to be used. List information to be provided to the subjects. Reference may be made to the Life Sciences Research Protocol. If a consent form is not required, so state.

8. Additional Attachments

- Updated safety certificates (inspection and certification of ground-based equipment should be performed annually).
- Updated Institutional Review Board certificates.
- Qualifications of new personnel.
- Equipment calibration record.

Guidelines for Radionuclide Use in Space Flight Payloads

The large number of permutations of radionuclide type, amount, chemical and physical form, and degree of containment requires that each experiment involving radionuclides be evaluated on its own merit. Nonetheless, some general guidelines can be set forth. These guidelines are not hard and fast and may be waived if other safety features or procedures are deemed adequate.

1. No payload containing radioactive material or other sources of ionizing radiation shall create a situation whereby:

   a. Radiation levels which, if an individual were continuously present in the area, could result in the individual's receiving a dose in excess of 2 millirems in any 1 hour, or

   b. Radiation levels which, if an individual were continuously present in the area, could result in the individual's receiving a dose in excess of 50 millirems in a 365-day period.

2. No payload or experiment, by design, shall cause quantities of radioactive material to be released into an occupied space which could result in uniform air concentrations in excess of the values specified in 10 CFR Part 20 - Appendix B. For calculation purposes, the volume of the crew compartment is 65 m^3 and that of the Spacelab is 77 m^3.
   The maximum permissible dose and the maximum permissible concentrations of radionuclides as recommended are primarily for the purpose of keeping the average dose to the individual members of the public as low as reasonably achievable (ALARA) and not because of the likelihood of specific injury to an individual.

   The annual occupational dose limit for radiation workers are: 5 rems for the total effective dose equivalent; 50 rems for the sum of the deep-dose equivalent to any individual organ or tissue other than the lens of the eye; 15 rems to the lens of the eye; and 50 rems to the skin or any extremity as shallow-dose equivalent. The ALARA principle should be applied to all experimental design.

   In no case should the accumulated occupational dose from radioactive material and external radiations to any crewmember exceed the monthly, annual, or career dose limits accepted by NASA.

3. General rules for safe use of radioactive materials shall be followed:

   - Wear disposable gloves and a surgical-type mask at all times while handling radioactive liquids or powders. The gloves should prevent contamination of the hands and a mask should reduce chances of inhalation and/or ingestion.

   - Do not eat or drink in any area where radioactive material is being used.

   - Wipe all work surfaces after use of radioactive materials.

- Practice good personal hygiene habits by always thoroughly cleaning hands after handling radioactive sources.

- Never mouth-pipette liquids containing radioactive materials. To the maximum extent possible minimize handling and transfers of radioactive materials in flight.

- Dispose of radioactive waste only in specifically designated receptacles that are properly shielded and labeled.

- Confine radioactive solutions, specimens, powders, and waste in double containment, plainly identified and labeled. Containment must be leakproof and puncture resistant. (Hood, glove box, or vented workbench could be considered one of the containers, but not stowage bins.)

- All transfers of radioactive liquids should be accomplished by the "buddy system." The individual performing the transfer will be assisted by an assistant to catch or trap droplets, aerosols, etc., with absorbent material to ensure that no trap droplets or aerosols are released into the occupied areas.

4. Contingency plans for all conceivable off-nominal situations shall be developed and tested.

5. Individuals trained in Health Physics shall be involved with the stowage, the post-mission handling of payloads utilizing radioactive materials capable of producing radioactive contamination, and post-mission survey for contamination of the spacecraft.

Adherence to the guidelines is important for radiological protection of the operator and other crewmembers in the Spacelab or crew compartment. Moreover, such adherence is important in minimizing contamination buildup in the spacecraft which can interfere with other investigators' experiments.

Useful Radiation Exposure Comparisons

Table 1. Magnitude of Radioactive Releases

EVENT (NUMBER)	LOCATION	YEAR(S)	CURIES RELEASED (TOTAL)	ISOTOPES	RISK (FATAL CANCERS)
Chernobyl	Ukraine, Soviet Union	1986	950,000 1,900,000 17,000,000	Cs-234; Cs-137; I-131	17,400 expected/ 2.9 billion exposed
Household radon	United States	Lifetime	N/A	Ra-222	14,000 per year expected/ 240 million
Atomic weapons testing (atmospheric)	Worldwide	1945-1980	~26 million (Cs-137); ~18 million (Sr-90); ~19 billion (I-131); ~6.5 billion (H-3); ~ 6 million (C-14)	Cs-137; Sr-90; I-131; H-3; C-14	12,000 expected/ 5 billion
First A-bombs	Hiroshima & Nagasaki, Japan	1945	~250,000,000	short-lived fission products	300 estimated/ 76,000 tracked
Early Hanford operations	Hanford, Washington	1945-1947	700,000	I-131	~1.6 cases of thyroid cancer expected/ 3,200
Three Mile Island	Harrisburg, Pennsylvania	1979	15 10,000,000	I-131; noble gases	0.7/ 2 million exposed
RaLa tests (254)	Los Alamos, New Mexico	1944-1962	250,000	La-140	0.4 cases/ 10,000 exposed
Green Run	Hanford, Washington	1949	8,000 20,000	I-131; Xe-133	0.04 expected/ 30,000 exposed
RW field tests (65)	Dugway, Utah	1949-1952	13,000	Ta-182	Unknown

Table 1, minus all footnotes, was reprinted from: Final Report - Advisory Committee on Human Radiation Experiments, October 1995, Chapter 11, Part II, p. 534 (Pittsburgh:US Government Printing Office).

Useful Radiation Exposure Comparisons

Table 2. Examples of Common Radiation Exposures

Radiation Exposure Source	Approximate Dose (rem)
Transcontinental Round Trip, Jet (New York - London; 37,000 ft)	0.004
Chest X-ray (Lung Dose)	0.010
Living One Year in Houston	0.100
Living One Year in Denver	0.200
Xeromammography (Breast Dose)	0.100
Barium Enema (Intestinal Dose)	0.875
Living One Year in Kerala India	1.300
Maximum Allowable in One Year to an Earth-based Radiation Worker	5,000
Maximum Allowable in One Year to a Space-based Radiation Worker	50,000

Table 3. Chest X-ray Standards
(Aviator Standards)

AGENCY	FREQUENCY OF CXR EXAM
NASA (Class I, II, III)	Every 5 years
Navy (Service Grade 1)	Age 21, 24, 27, 30, 36, 39, and annually at 40 and older
Air Force (Class I, II, III, ACC)	Only when clinically indicated
Army	Only when clinically indicated
FAA (Class I, II, III)	Only when clinically indicated
Russian Military	Every year (ref: Oleg Ryumin, MD)
Russian Cosmonauts	Every year (ref: Oleg Ryumin, MD)
US Previous Service Task Force	Not recommended as screening method for asymptomatic patient
American Cancer Society	Not recommended as screening method for asymptomatic patient

Table 4. Chest X-ray Doses at JSC Clinic

TYPE	DOSE	WHOLE BODY DOSE EQUIVALENT
PA; 90-100 kVp	4-8 mrem	Male: 1.64 mrem Female: 1.08 mrem
Lateral; 120-125 kVp	13-30 mrem	Male: 5.77 mrem Female: 3.61 mrem
Average dose	*17 mrem*	

IONIZING RADIATION SOURCE DATA SHEET
SPACE FLIGHT HARDWARE AND APPLICATIONS

Lyndon B. Johnson Space Center

Complete Items 1 through 10 and Part A for radioisotope sources and Part B for ionizing radiation-producing equipment.

IDENTIFICATION

1. PAYLOAD DESIGNATION/EXPERIMENT	2. STS NUMBER AND/OR LAUNCH DATE
3. SOURCE USING ORGANIZATION	4. ADDRESS
5. CONTACT	6. TELEPHONE
7. PAYLOAD SPONSOR/MANAGER	8. ADDRESS
9. CONTACT	10. TELEPHONE

PART A. RADIOISOTOPE SOURCES

I. SOURCE DESCRIPTION

ISOTOPE	TOTAL QUANTITY *(MILLICURIE)* *(Include determination date)*	NUMBER OF SOURCES *(List individual source quantity)*

CHEMICAL FORM	PHYSICAL STATE
SOURCE SEALED ☐ YES ☐ NO	IDENTIFICATION NUMBERS
MANUFACTURER	ADDRESS

II. SOURCE USE DATA

PURPOSE

☐ EXTERNAL CALIBRATION ☐ INFLIGHT CALIBRATION

☐ OTHER *(Describe)*

☐ CREW INVOLVEMENT/REQUIREMENTS *(Include nominal and contingent situations)*

III. SOURCE DIAGRAM

DETAILS ON SEALING, TECHNIQUES, AND DIMENSIONS

IV. TEST DATA

DATA SOURCE LEAK TESTED	RESULTS (MICROCURIE)

THERMO-VACUUM QUALIFIED TO:	DATE
_____ MM Hg _____ DEGREE C.	

V. PRE-FLIGHT TRANSFERS

LOCATIONS WHERE SOURCE IS TO BE USED OR STORED AND APPROXIMATE DATES

LOCATIONS	DATED FROM:	TO:

SOURCE CUSTODIAN/RADIATION SAFETY OFFICER	TELEPHONE

VI. POST-FLIGHT DISPOSITION

OUTLINE REQUIREMENTS

PART B. IONIZING RADIATION PRODUCING EQUIPMENT

I. EQUIPMENT CHARACTERISTICS

TYPE OF RADIATION PRODUCED

MAXIMUM ENERGY LEVEL	OPERATING ENERGY LEVEL

DURATION OF OPERATION	NO. OF UNITS	PULSED UNIT DUTY CYCLE
_____ HOURS TOTAL, ALL UNITS		

II. RADIATION CHARACTERISTICS

RADIATION INTENSITY OF FLIGHT CONFIGURED UNIT	SECONDARY RADIATIONS PRODUCED	
	ENERGY LEVEL	TYPE
_____ RAD/HR @ _____ METERS	_____ KeV	

III. EQUIPMENT USE DATA

CREW INVOLVEMENT/PROCEDURES

RADIATION PRODUCTION WARNING SYSTEM	SAFETY INTERLOCK SYSTEM
☐ YES *(Describe)* ☐ NO	☐ YES *(Describe)* ☐ NO

RADIO FREQUENCY/MICROWAVE HAZARD EVALUATION DATA

(PLEASE TYPE OR PRINT LEGIBLY)

NAME	ORGANIZATION/MAIL CODE	DATE	REFERENCE NO.

I. SYSTEM DESCRIPTION

A. SYSTEM DESIGNATION	B. TYPE OF SYSTEM	C. LOCATION OF USE	QUANTITY

D. SYSTEM CHARACTERISTICS/CAPABILITIES

1. Fixed, mobile or temporary system: _____
2. Size, type, and quantity of antennas: _____
3. Height above occupied areas: _____
4. Azimuth capability: _____
5. Elevation capability: _____
6. Azimuth stops: _____
7. Elevation stops: _____
8. Type transmission lines: _____
9. Qty. and type power tubes: _____
10. Peak voltage to tubes: _____
11. Interlocked doors to H.V. Cab: _____
12. Frequency capability: _____

E. OPERATING PARAMETERS (Indicate parameters used for normal operations)

1. Continuous or pulsed emission: _____
2. Pulse width(s): _____
3. Pulse repetition frequency: _____
4. Pulse code: _____
5. Maximum rated duty cycle: _____
6. Normal operating frequency: _____
7. Peak power to transmitter: _____
8. Insertion loss (transmitter to antenna): _____
9. Antenna gain: _____
10. Type of illumination: _____
11. Beam width/skew: _____
12. Polarization of transmitted wave: _____
13. Scan rate (RPM): _____
14. Estimated hazard distance (meters): _____

II. AREA DESCRIPTION

A. Bldg. no: _____ Room no.: _____

B. Site plans: _____

C. System drawings: _____

D. Adjacent areas/facilities: _____

(Submit copies as attachments)

III. PROCEDURES

A. Operating procedures: _____

B. Accident/emergency proc.: _____

C. Maintenance procedure: _____

D. Brief description of project: _____

(Submit copies as attachments)

IV. SYSTEM USERS

A. User org.: _____ B. Maint. org.: _____

C. Area radiation officer: _____

V. PERIOD OF USE

From: _____ To: _____

VI. RADIATION PROTECTION REQUIREMENTS

- ☐ Accountability
- ☐ Compliance with ACGIH TLV's
- ☐ Compliance with JPD 1860.4
- ☐ Other

VII. REVIEW

(Radiation Safety Use)

Additional Information Required: Yes _____ No _____ Date Received: _____

Disposition: _____

JSC Radiation Safety Officer Signature	Recommend ☐ Approval ☐ Disapproval	Date:
JSC Radiation Safety Committee Chairperson Signature	☐ Approved ☐ Disapproved	Date:

JSC Form 44A (Rev May 96) (MS Word May 96)

Appendix I

LASER/OPTICAL DEVICE HAZARD EVALUATION DATA

(Please type/print legibly)

Name	Mail Code	Date	Reference No.

I. LASER DESCRIPTION

A. Type of Laser Media	B. Manufacturer	C. Model No. and Year	D. Serial No.	E. ANSI Class

F. Emission Characteristics *(Use supplemental sheets as needed)*

Mode of Operation	Peak Power	Pulse Width Sec.	PRF	Wavelength(s)*	Max. Exposure Time	Beam Dia. @ i/e (cm)	Beam Div. @ i/e (rad)

*For multiple wavelength lasers, specify power levels of individuals wavelength

II. OPTICAL DEVICE DESCRIPTION

A. Type Device	B. Manufacturer	C. Model No. and Year	D. Serial No.

E. Operating characteristics (including power output, wavelength(s), dimensions associated with optics where applicable, etc.)

III. AREA DESCRIPTION

A. Location: _____
B. Site Plans: _____
C. System Drawings: _____
D. Adjacent Areas/Facilties: _____

(Submit copies as attachments)

IV. PROCEDURES

A. Operating Procedures: _____
B. Accident/Emergency Proc.: _____
C. Maintenance Procedure: _____
D. Brief Description of Project: _____

(Submit copies as attachments)

V. HAZARD ANALYSIS

A. ANSI MPE: _____ B. Eyewear O.D. Required: _____
C. @ Wavelength: _____
D. Estimated Hazard Zones: Direct Beam: _____ m Lens: _____ m
Diffuse: _____ m Other: _____ m

VI. SYSTEM USERS

A. User Org.: _____
B. Maint. Org.: _____
C. Area Radiation Officer: _____

VII. RADIATION PROTECTION REQUIREMENTS

☐ Accountability
☐ Compliance with Am. Nat'l. Standards Institute (ANSI) Safety Levels
☐ Compliance with JPD 1860.4

VIII. REVIEW

Additional Information Required: ☐ YES ☐ NO Date Received: _____
Disposition: _____

JSC Radiation Safety Officer Signature	Recommend ☐ Approval ☐ Disapproval	Date:
JSC Radiation Safety Committee Chairperson Signature	☐ Approved ☐ Disapproved	Date:

JSC Form 44B (Rev May 96) (MS Word May 96)

WORKSHEET FOR TISSUE DOSES FROM RADIOPHARMACEUTICALS

This form is to be used for each radionuclide and individual receiving radiopharmaceuticals. For reference information see Report 53 of the International Commission on Radiological Protection, *Radiation Dose to Patients from Radiopharmaceuticals*. Annals of the ICRP, Vol 18(1-4), 1987.

Principal Investigator and Address	Radiopharmaceutical

Brief Title of Study

Tissue	Absorbed dose per unit activity (mrad/microcurie) or (mGy/MBq)	Total radioactivity administered (microcurie) or (MBq)	Tissue absorbed dose (mrad) or (mGy)
Adrenals			
Bladder			
Bone			
Breast			
Stomach			
Small intestine			
Upper large intestine			
Lower large intestine			
Kidneys			
Liver			
Lungs			
Ovaries			
Pancreas			
Red marrow			
Spleen			
Testes			
Thyroid			
Uterus			
Skin			
Eyes			
Effective dose equivalent			

JSC Form 44C (Rev May 96) (MS Word May 96)

WORKSHEET FOR TISSUE DOSES FROM DIAGNOSTIC X-RAY EXAMINATIONS

This form is to be used for each projection and view to be performed on each individual. For reference information see HHS Publication (FDA) 89-8031, *Handbook of Selected Tissue Doses for Projections Common in Diagnostic Radiology*, Center for Devices and Radiological Health, Rockville, Maryland 20857.

Principal Investigator and Address	Projection and View

Brief Title of Study

Tissue	Skin entrance exposure (R)	Tissue dose (mrad) or (mGy)
Adrenals		
Bladder		
Bone		
Breast		
Stomach		
Small intestine		
Upper large intestine		
Lower large intestine		
Kidneys		
Liver		
Lungs		
Ovaries		
Pancreas		
Red marrow		
Spleen		
Testes		
Thyroid		
Uterus		
Skin		
Eyes		
Effective dose equivalent		

JSC Form 44D (Rev May 96) (MS Word May 96)

RADIOPHARMACEUTICAL HUMAN USE INFORMATION FORM

Organization	☐ New Request ☐ Modification	Date prepared

Title or brief description of project

Name and address of principal investigator	U.S. N.R.C. and/or state license no.	☐ Yes ☐ No Authorized to use proposed nuclides with given license?
Name and license of attending physician	License expiration date	☐ Yes ☐ No Has the use of non-radioactive materials been investigated?

Pre-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Location (NASA Center, bldg. no., room) and frequency or flight-days of usage (ex: L-90)

In-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Flight days, mission elapsed time (MET) and usage location on orbiter

Post-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Location (NASA Center, bldg. no., room) and frequency or flight-days of usage (ex: R+2)

JSC Form 44E (May 96) (MS Word May 96)

RADIOPHARMACEUTICAL UNIT DOSAGE RECEIPT AND USE LOG

Authorized User: _____

Study: _____ Radiopharmaceutical: _____

Date Received	Supplier	Lot No.	Dosage (microcurie)	Label Time	Date Dispensed	Time Dispensed	Measured (microcurie)	Subject	Init.

JSC Form 44F (May 96) (MS Word May 96)

RADIOPHARMACEUTICAL MULTIDOSE VIAL PREPARATION AND USE LOG

Authorized User: _____

Study: _____ Radiopharmaceutical: _____

Date Prepared	Time	Date Generator Received	Kit Manufacturer	Kit Lot No.	microcurie/cc	cc	Measured (microcurie)	Subject	Init.

JSC Form 44G (May 96) (MS Word May 96)

This page intentionally left blank.

Appendix I

RADIOACTIVE MATERIAL USE AUTHORIZATION			REF. NO.
Request Originator *(Please Type)*	Organization	☐ New Request ☐ Modification	Date

1. Description of Proposed Use *(Additional information may be attached.)*

2. Written Procedures and Safety Precautions *(Submit as an attachment.)*	3. Completion Date

4. Location of Use

a. Site ☐JSC ☐WSTF ☐Other	b. Building	Room

If other, submit data for the site location, written authorization, and a copy of its license, if available.

c. Laboratory Classification

d. Will radioactive waste be generated? (If yes, attach the WASTE PROFILE) ☐ Yes ☐ No

e. Will this proposed use generate airborne radioactive material? ☐ Yes ☐ No

f. Is radiation monitoring equipment accessible to the users? ☐ Yes ☐ No

5. Radioactive Material Requirements

a. Element and Isotope	b. Millicurie Activity per Experiment	c. Physical Form			d. Leak test required?		e. Maximum Amount at one time. Millicurie(s)
		solid	liquid	gas	Yes	No	

6. Submit a JSC 1944, Radiation User Approval form for each proposed user.

7. Area Responsible User	a. Area Responsible User Signature	b. Telephone No.	c. Mail Code

8. NASA Technical Manager or NASA Supervisor Signature	a. Title or Position	b. Telephone No.

9. JSC Radiation Safety Committee Action	Date

☐ Approved ☐ Approved, Subject to Conditions Noted in Item 10 ☐ Disapproved

JSC Radiation Safety Committee Chairperson Signature	Radioactive Material Use Authorization Expiration Date

10. This Use Authorization shall be subject to all applicable rules, regulations, and orders of the JSC Radiation Safety Committee now or hereafter in effect along with the specified below:

a) Standard Conditions
   (1) The responsible authorized user shall insure compliance with JPD 1860.2, Radiological Health Manual, and with the statements and procedures contained within this request.
   (2) Additionally, the responsible authorized user shall provide for the security and control of the radioactive material and for training of radiological health and safety precepts to each individual using such radioactive material

b) Special Conditions (Required by the Radiation Safety Committee): _____

_____

JSC Form 1942 (Rev May 96) (MS Word May 96) Page 1 of 2

INSTRUCTIONS FOR JSC FORM 1942

Reference Number: Leave blank. To be filled in by Radiation Safety Office.

Request Originator and Organization: Self-explanatory.

New Request: Initial submittal or major rewrite.

Modification: For renewal or minor changes in users, location, etc.

1. Title and objective of project.

2. Include special techniques, safety precautions, labeling and safe practice statements along with the inhouse training and posting information to be made available to area employees conducting this task. The following should be considered:

Are general procedures written and posted?
Are emergency procedures written and posted?
What are the methods of containment (hoods, spill trays, absorbents, work surfaces, floors, etc.)?
What is estimated waste activity/gram of media? How is the waste to be handled and documented?
Is there controlled access to use area?
What are the proposed training and requirements for assistants and peripheral personnel?
What considerations are given to women of child-bearing age and pregnant women?

3. Enter date if one-time only. For a continuous operation, enter the day's date plus one year.

4a. *Other* refers to temporary job site. Does not include buildings leased or located outside JSC or White Sands location fences. The use of temporary job sites requires advanced written approval from that location's management. If the job site has a state or federal license for radioactive material, so note.

4b. If multiple locations, list all.

4c. Required only if the proposed use is for radioisotopes in liquid form. Consult with the Radiation Safety staff to determine the proper classification for the laboratory or use location.

4d. If yes, attach a waste profile identifying any EPA-classified hazardous waste, and a summation of total activity with a separate breakdown of microcuries/grams of material.

5a. List all isotopes needed.

5b. How much activity will be utilized per each one-time use?

5c. If different for each isotope, identify each form as gas, liquid, sealed, plated, powder, solid.

5e. What is the maximum activity the area will contain at any one time, for each isotope? This total should include stock solutions in the area.

6. Attach a Radiation User Approval form (JSC Form 1944) for each person who will use or handle the radioactive material. The JSC Radiation Safety Committee will review each application to determine if the requester qualifies as an "authorized user". Each "authorized user" must have a minimum of a B.S. degree and 40 hours of radiation safety training, or equivalent job-related experience and training. Training must include the use of radiation detection instrumentation, and the biological hazards of exposure to radiation appropriate to the types and forms of radioactive materials requested. Additional requirements are identified in the Code of Federal Regulations 10 CFR Part 35.910, when radiopharmaceuticals are to be administered to human subjects.

7. Area Responsible User - refers to the individual that will be responsible for overall compliance with the requirements set forth by the JSC Radiation Safety Committee's approval of this Radioactive Material Use Authorization request.

a. Area Responsible User signature
b. Telephone number of the Area Responsible User
c. Mail Code of the Area Responsible User

9-10. Leave blank.

All questions should be directed to SD23/Radiation Safety Office, Building 229, Extension 37082.

RADIATION USER APPROVAL

Please Type

Name _____ Telephone Number _____

Employer _____ Mail Code _____

Proposed Radiation Use _____

List Isotopes _____ Total Activity (millicuries) _____

RADIATION TRAINING

	FORMAL	INFORMAL	NO. OF HOURS	LOCATION
1. Principles and practices of radiation protection.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____
2. Radioactivity measurements standardization and monitoring techniques and instruments.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____
3. Biological effects of radiation.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____

Have you had forty hours of radiation training? ☐ Yes ☐ No Are you an M.D.? ☐ Yes ☐ No

EXPERIENCE

(Check applicable area(s))

An "authorized user" on license no. _____ ☐ NRC ☐ State ☐ Certified in medical X-ray

☐ Administered isotopes to humans ☐ Used radiation monitoring equipment

☐ X-ray machine(s) ☐ Radioactive material ☐ College lab isotopes ☐ Multi-Curie sources

☐ Certified in radiography ☐ Radiation exposure limits ☐ Gas chromatography source(s)

☐ Other Explain _____

Nuclide(s) _____ Amount Curie(s) _____ X-ray Equipment Output kvp _____

Purpose _____

Location(s) _____

Duration _____

I certify that I have read the following:

1. NRC Regulations, Parts 19 and 20, and OSHA 1910.96
2. Radiological Health Manual. (JPG 1860.2)
3. Local Procedures and Methods of Control.

Date _____

Signature _____
(Requester)

JSC Radiation Safety Committee Action:

Approved ☐ Yes ☐ No

Date _____

Signature _____
Chairperson, JSC Radiation Safety Committee

Special Conditions _____

Attach additional information if necessary

JSC Form 1944 (May 96) (MS Word May 96)

National Aeronautics and
Space Administration

Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

Reply to Attn of: SA-95-IRB Renewal

NASA-JSC INSTITUTIONAL REVIEW BOARD (IRB)

PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

Use this form only to request annual renewal of an existing protocol. All information must be typed.

PROTOCOL NUMBER: _____

PREVIOUS APPROVAL PERIOD FROM: _____ TO _____

PROTOCOL TITLE: _____

IRB CONTACT: Ms. Mary Flores
PHONE: (713) 212-1468
MAIL CODE: KRUG PM/P2

E-MAIL: Flores, Mary
FAX: (713) 212-1465
ADDRESS: KRUG Life Sciences
Houston, TX 77058

INVESTIGATOR: _____
PHONE: _____
MAIL CODE: _____
DIVISION: _____

E-MAIL: _____
FAX: _____
ADDRESS: _____

National Aeronautics and
Space Administration

Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

Reply to Attn of:

SA-95-IRB-Renewal 2

NASA-JSC INSTITUTIONAL REVIEW BOARD (IRB)

PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

SPONSOR: (funding source): _____

Total number of subjects request to complete study: _____
Is this research project still enrolling subjects: ( ) YES ( ) NO
If no, when did enrollment end? _____

Total number subjects enrolled in study to date: Male _____ Female _____
How many subjects did you enroll during the last review period? Male _____ Female _____

Number of withdrawls to date: _____
General reason(s) for withdrawl: _____
_____

Number of adverse events to date: _____
Summary of adverse events (note significant AE's): _____
_____
_____
_____
_____

Preliminary results of study: _____
_____
_____

Considering your preliminary results, re-state the risk/benefit ratio: _____
_____
_____

National Aeronautics and
Space Administration

Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

Reply to Attn of: SA-95-IRB-Renewal 3

NASA-JSC INSTITUTIONAL REVIEW BOARD (IRB)

PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

Since the last approval have there been additions or deletions of co-investigators that have not already been communicated to the Board? ( ) YES ( ) NO
If yes, list: _____

_____

_____

ATTACHMENTS

Consent Form

O The form must conform to the NASA guidelines

Budget

O For renewal attach a copy of the remaining budget for the project

_____
I certify that all information is correct.

_____ _____
Signature of Principal Investigator (original signature only) Date

Other signatures:

_____ _____
Division Chief Date

_____ _____
Branch Chief Date

This page intentionally left blank.

NASA/JSC HUMAN RESEARCH INFORMED CONSENT *

1. I, the undersigned, do voluntarily give my informed consent for my participation as a test subject in the following research study, test, investigation, or other evaluation procedure:

NAME OF INVESTIGATION _____

_____

FLIGHT TO WHICH ASSIGNED _____

PRINCIPAL INVESTIGATOR _____

RESPONSIBLE NASA PROJECT SCIENTIST _____

I understand or acknowledge that :

(a) This procedure is part of an investigation approved by NASA.

(b) I am performing these duties as part of my employment with _____.

(c) This research study has been reviewed and approved by the JSC Institutional Review Board (IRB) which has also determined that the investigation involves _____ risk to the subject.
(minimal or reasonable)

(d) Definitions:

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

"Reasonable risk" means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

(e) The research procedures were explained to me prior to the execution of this form. I was afforded an opportunity to ask questions, and all questions asked were answered to my satisfaction. A layman's description was provided to me. **

(f) I am medically qualified to participate in the investigation.

(g) I know that I can refuse to participate in the tests at any stage of their performance, and my refusal will be honored, except in those cases when, in the opinion of the responsible physician, termination of the tests could have detrimental consequences for my health and/or the health of the other subjects. I further understand that my withdrawal or refusal to participate in this investigation will not result in any penalty or loss of benefits to which I am otherwise entitled.

(h) In the event of physical injury resulting from this study and calling for immediate action or attention, NASA will provide or cause to be provided, the necessary treatment. I also

understand that NASA will pay for any claims of injury, loss of life or property damage to the extent required by the Federal Employees Compensation Act or the Federal Tort Claims Act. My agreement to participate shall not be construed as a release of NASA or any third party from any future liability which may arise from, or in connection with, the above procedures.

(i) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of my participation as a research subject in this study shall be maintained so that no data may be linked with me as an individual. I understand, however, that if a "life-threatening" abnormality is detected, the investigator will notify me and the JSC Flight Medicine Clinic. Such information may be used to determine the need for care or medical follow-up, which, in certain circumstances, could affect my professional (flight) status.

Signature: Signature:

Test Subject Date Witness Date

2. I, the undersigned, the Principal Investigator of the investigation designated above, certify that:

(a) I have thoroughly and accurately described the research investigation and procedures to the test subject and have provided him/her with a layman's description of the same.

(b) The test setup involves _____ risk to the test subject. All equipment to
(minimal or reasonable)

be used has been inspected and certified for safe and proper operation.

(c) The test subject is medically qualified to participate.

(d) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of the test subject's participation in this study shall be maintained so that no data may be linked to him/her as an individual.

(e) The test protocol has not been changed from that originally approved by the JSC IRB.

Signature: Signature:

Principal Investigator Date NASA Project Scientist Date

Notes:

* This form is valid for the period including preflight, in-flight, and postflight data collection sessions for the mission. Before the first baseline data collection, the Principal Investigator

will repeat the briefing concerning risks involved in the investigation. A signed, dated copy of this form with attachments must be forwarded to Chairperson, Johnson Space Center Institutional Review Board, Attn: Dr. Lawrence Dietlein, Mail Code SA, Lyndon B. Johnson Space Center, Houston, Texas 77058.

** A detailed description of the investigation will be attached to this consent form. The Principal Investigator is responsible for formulating this document, which should be in layman's terms such that the subject clearly understands what procedures will be required of him/her and the risks associated therewith.

The detailed description of the research must, at a minimum, include the following:

(1) An explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject, including, but not limited to, possible adverse reactions of all medications to be administered and any risks/hazards resulting from exposure to ionizing radiation;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) Clarification of all forms of behavior, if any, interdicted by the research protocol (e.g., exercise, diet, medications, etc.); and

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

When appropriate, the following information shall also be provided in the detailed description:

(8) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(9) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(10) Any additional costs to the subject that may result from participation in the research;

(11) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(12) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(13) The approximate number of subjects involved in the study.

Appendix K

NASA/RSA HUMAN RESEARCH INFORMED CONSENT *

1. I, the undersigned, do voluntarily give my informed consent for my participation as a test subject in the following research study, test, investigation, or other evaluation procedure:

NAME OF INVESTIGATION _____

_____

FLIGHT TO WHICH ASSIGNED _____

PRINCIPAL INVESTIGATOR _____

RESPONSIBLE NASA PROJECT SCIENTIST _____

RESPONSIBLE RSA SCIENCE PROGRAM MANAGER _____

I understand or acknowledge that :

(a) This procedure is part of an investigation approved by NASA/RSA.

(b) I am performing these duties as part of my employment with _____.

(c) This research study has been reviewed and approved by the JSC Institutional Review Board (IRB) and the Russian Biomedical Ethics Board which have also determined that the investigation involves _____ risk to the subject.
(minimal or reasonable)

(d) Definitions:

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

"Reasonable risk" means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

(e) The research procedures were explained to me prior to the execution of this form. I was afforded an opportunity to ask questions, and all questions asked were answered to my satisfaction. A layman's description was provided to me. **

(f) I am medically qualified to participate in the investigation.

(g) I know that I can refuse to participate in the tests at any stage of their performance, and my refusal will be honored, except in those cases when, in the opinion of the responsible physician, termination of the tests could have detrimental consequences for my health and/or the health of the other subjects. However, understanding the significance of the investigations (tests), I will give every effort to perform the full scope of the program.

(h) In the event of injury resulting from this study, I understand that I will receive medical attention and necessary treatment. I also understand that I will be compensated for any injuries to the extent permitted under current U.S. and Russian laws and provisions of

the contract between NASA and RSA. My agreement to participate shall not be construed as a release of NASA/RSA or any third party from any future liability which may arise from, or in connection with, the above procedures.

(i) Consistent with statutory and Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of my participation as a research subject in this study shall be maintained, so that no data may be linked with me as an individual. However, if a "life-threatening" abnormality is detected, the investigator will notify me and the JSC Flight Medicine Clinic. Such information may be used to determine the need for care or medical follow-up, which, in certain circumstances, could affect my professional (flight) status.

Signature:

_____

Test Subject Date

2. I, the undersigned, the Principal Investigator of the investigation designated above, certify that:

(a) I have accurately described the procedure to the test subject.

(b) The test setup involves _____ risk to the test subject. All equipment to
(minimal or reasonable)

to be used has been inspected and certified for safe and proper operation.

(c) The test subject is medically qualified to participate.

(d) The test protocol has not been changed from that originally approved by the JSC IRB and the Russian Biomedical Ethics Board.

Signature:

_____

Principal Investigator Date

Concurrence:

_____

NASA Project Scientist Date

Concurrence:

_____

RSA Science Program Manager Date

Notes:

* This form is valid for the period including preflight, in-flight, and postflight data collection sessions for the mission. Before the first baseline data collection, the Principal Investigator will repeat the briefing concerning risks involved in the investigation. A signed, dated copy

of this form with attachments must be forwarded to 1) Chair, Johnson Space Center Institutional Review Board, ATTN: Dr. Lawrence Dietlein, Mail Code SA, Lyndon B. Johnson Space Center, Houston, Texas 77058, and 2) The Institute for Biomedical Problems, ATTN: Dr. Abram Genin, Biomedical Ethics Commission, Khoroshevskoe shosse, 76A, Moscow, 123007, Russia.

** A detailed description of the investigation will be attached to this consent form. The Principal Investigator is responsible for formulating this document, which should be in layman's terms such that the subject clearly understands what procedures will be required and the risks associated therewith.

The detailed description of the research procedures must specifically list the risks associated with the procedures to be employed, the possible adverse reactions of all medications to be administered, and the risks/hazards resulting from exposure to ionizing radiation. Further, the investigator must clearly specify all forms of subject behavior interdicted by the research protocol (exercise, diet, medication, etc.).

National Aeronautics and
Space Administration

Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

Reply to Attn of: SA-96-IRB

[Date]

Principal Investigator
Address
Mail Code

RE: Title of Investigation

Approval valid from [Date] to [Date]

Dear [Principal Investigator]:

1. The Johnson Space Center (JSC) Institutional Review Board (IRB) has taken the following action with respect to the above named proposal:

( ) Proposal is approved as written for 1-year by Board consensus or majority vote
( ) Proposal approved pending incorporation of Board minor suggestions, modifications, or recommended actions
( ) Proposal tabled pending incorporation if significant modifications and/or recommendations of Board into original proposal for subsequent final review
( ) Proposal rejected)vote listed in minutes)
( ) Medical monitoring designation; ( ) Not Required; ( ) Level I; ( ) Level II; ( ) Level III; ( ) Level IV

2. Additional review of this proposal will be required:

( ) a. Annually
( ) b. If there is any substantive change in protocol
( ) c. Should unexpected problems or unusual complications develop in executing the protocol
( ) d. Other _____

3. Method of review utilized:

( ) a. Scientific Merit Review Committee prior to JSC IRB
( ) b. JSC Institutional Review Board
( ) c. Expedited Review

_____ _____
Lawrence F. Dietlein, M.D., Ph.D. Date
Chairperson, JSC Institutional Review Board

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
INVESTIGATIONAL NEW DRUG APPLICATION (IND)
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) Part 312)

Form Approved: OMB No. 0910-0014. Expiration Date: November 30, 1995. See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR

2. DATE OF SUBMISSION

3. ADDRESS (*Number, Street, City, State and Zip Code*)

4. TELEPHONE NUMBER (*Include Area Code*)

5. NAME(S) OF DRUG (*Include all available names Trade, Generic, Chemical Code*)

6. IND NUMBER (*If previously assigned*)

7. INDICATION(S) (*Covered by this submission*)

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED. [ ] PHASE 1 [ ] PHASE 2 [ ] PHASE 3 [ ] OTHER_____ (*Specify*)

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (*21 CFR PART 312*), NEW DRUG OR ANTIBIOTIC APPLICATIONS (*21 CFR PART 312*), DRUG MASTER FILES (*21 CFR 314.420*), AND PRODUCT LICENSE APPLICATION (*21 CFR PART 601*) REFERRED TO IN THIS APPLICATION

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial Number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER: — — —

11. THIS SUBMISSION CONTAINS THE FOLLOWING. (*Check all that apply*)

[ ] INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
[ ] RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S)
[ ] NEW PROTOCOL
[ ] CHANGE IN PROTOCOL
[ ] NEW INVESTIGATOR

INFORMATION AMENDMENT(S)
[ ] CHEMISTRY/MICROBIOLOGY
[ ] PHARMACOLOGY/TOXICOLOGY
[ ] CLINICAL

IND SAFETY REPORT(S)
[ ] INITIAL WRITTEN REPORT
[ ] FOLLOW-UP TO A WRITTEN REPORT

[ ] RESPONSE TO FDA REQUEST FOR INFORMATION
[ ] ANNUAL REPORT
[ ] GENERAL CORRESPONDENCE

[ ] REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
[ ] OTHER_____ (*Specify*)

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECK BELOW. REFER TO CITED CFR SECTION FOR FURTHER INFORMATION.
[ ] TREATMENT IND 21 CFR 312.35(B) [ ] TREATMENT PROTOCOL 21 CFR 312.35(A) [ ] CHARGE REQUEST/NOTIFICATION 21 CFR 312.7(D)

FOR FDA USE ONLY

CDR/DBIND/OGD RECEIPT STAMP	DDR RECEIPT STAMP	IND NUMBER ASSIGNED:
		DIVISION ASSIGNMENT:

PREVIOUS EDITION IS OBSOLETE

12. **CONTENTS OF APPLICATION**

This application contains the following items: (check all that apply)

[ ] 1. Form FDA 1571 *[21 CFR 312.23 (a) (1)]*

[ ] 2. Table of contents *[21 CFR 312.23 (a) (2)]*

[ ] 3. Introductory statement *[21 CFR 312.23 (a) (3)]*

[ ] 4. General investigational plan *[21 CFR 312.23 (a) (3)]*

[ ] 5. Investigator's brochure *[21 CFR 312.23 (a) (5)]*

6. Protocol(s) *[21 CFR 312.23 (a) (6)]*

- [ ] a. Study protocol(s) *[21 CFR 312.23 (a) (6)]*
- [ ] b. Investigator data *[21 CFR 312.23 (a) (iii) (b)]* or completed form(s) FDA 1572
- [ ] c. Facilities data *[21 CFR 312.23 (a) (6) (iii) (b)]* or completed Form(s) FDA 1572
- [ ] d. Institutional Review Board data *[21 CFR 312.23 (a) (6) (iii) (b)]* or completed Form(s) FDA 1572

[ ] 7. Chemistry, manufacturing, and control data *[21 CFR 312.23 (a) (8)]*

[ ] Environmental assessment or claim for exclusion *[21 CFR 312.23 (a) (7) (iv) (e)]*

[ ] 8. Pharmacology and toxicology data *[21 CFR 312.23 (a) (7)]*

[ ] 9. Previous human experience *[21 CFR 312.23 (a) (9)]*

[ ] 10. Additional information *[21 CFR 312.23 (a) (10)]*

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? [ ] YES [ ] NO

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? [ ] YES [ ] NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set forth in 21 CFR Part 56 will be responsible for the initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	
18. ADDRESS (*Number, Street, City, State and Zip Code*)	19. TELEPHONE NUMBER (*Include Area Code*)	20. DATE

(Warning: A willfully false statement is a criminal offense JSC Title 18 Sec 1001)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

PHS Reports Clearance Officer
Paperwork Reduction Project 0910-0014
Hubert H. Humphrey Building, Room 737-F
200 Independence Avenue, S.W.
Washington, DC 20201

Please DO NOT RETURN this application to this address.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
STATEMENT OF INVESTIGATOR
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) Part 312)
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014.
Expiration Date: November 30, 1995.
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED:

[ ] CURRICULUM VITAE [ ] OTHER STATEMENT OF QUALIFICATIONS

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED.

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY.

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES).

6. NAMES OF THE SUBINVESTIGATORS (*e.g., research fellows, residents, associates)* WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S).

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

[ ] FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED.

[ ] FOR PHASE 2 OR 3 INVEST ONS, AND OUTLINE OF THE STUDY PROTOCOL INCLUDING AN APPROXIMATION OF THE NUMBER OF SUB BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY; THE C USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION; THE KIN CAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF DY; AND COPIES OR A DESCRIPTION OF CASE REPORT FORMS TO BE USED.

9. COMMITMENTS:

I agree to conduct the study(ies nce with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, exce essary to protect the safety, rights, or welfare of subjects.

I agree not personally conduct or ne described investigation(s).

I agree to inform any patients, or ns used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Par e met.

I agree to report to the sponsor adve experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64.

I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continu review approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activ and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR:

1. **Complete all sections. Attach a separate page if additional space is needed.**

2. **Attach curriculum vitae or other statement of qualifications as described in Section 2.**

3. **Attach protocol outline as described in Section 8.**

4. **Sign and date below.**

5. **FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.**

10. SIGNATURE OF INVESTIGATOR	11.DATE

Request for Human Test Subject Recruiting

Date Submitted: _____

This form should be completed, approved by the appropriate Laboratory Supervisor and Principal Investigator, and submitted to the Human Test Subject Facility Recruiter, 483-7284, with the JSC IRB letter of approval prior to the start of subject recruitment for a study. Please allow sufficient time (typically six weeks) for the initial phase of recruiting. If newspaper advertising will be necessary, more time will be needed. Any changes to this form should be in writing. If a second group of test subjects is needed after the first group completes the study, an additional request for test subjects must be submitted in sufficient time for new recruitment.

Principal Investigator: _____ Telephone No.: _____ Mail Code: _____

Requester: _____ Telephone No.: _____ Mail Code: _____

Study Name: _____

Short version of study name: _____

The purpose of this study is: _____

Job order number the test subject pay will be charged to: _____

Projected study schedule: From: _____ To: _____

Study description: (Will there be hospital admissions, length of stay, any invasive procedures, special diet, etc.)?

Subject qualifications: (Age, weight, height, sex, etc.) _____

Drug study description: (Include information test subjects would be interested in knowing about the drug)

Specific subject information requirements: (Medications not permitted, fitness level, smoking habits, etc.)

Comprehensive drug screen is mandatory for all bedrest studies: (illicit drugs, prescription drugs, nicotine, alcohol, caffeine, etc.) Does this study require a comprehensive screen? _____

Payment of test subjects: (Total study pay, daily pay, etc.) _____

Approximate radiation exposure during this study: _____ (mrem)

Name of subjects: Male _____ Female _____

Sessions per subject: _____ Hours per session: _____

Laboratory Supervisor		Principal Investigator	
Signature	Date	Signature	Date

JOHNSON SPACE CENTER
MANAGEMENT
INSTRUCTION

JMI 7170.2A
Effective Date: January 31, 1996
Expiration Date: Until Rescinded

Responsible Office: SA

Subject: SCIENTIFIC MISCONDUCT WITH REGARD TO HUMAN RESEARCH

1. PURPOSE. To define the policy with regard to scientific misconduct as it applies to human research.

2. REFERENCES.

   a. NASA Management Instruction (NMI) 7100.8, "Protection of Human Research Subjects."

   * b. JSC Handbook (JHB) 1107.1, "The JSC Organization."

   c. JSC Management Instruction (JMI) 1382.5, "Maintaining the Privacy of Biomedical Research Data."

   d. JMI 7170.3, "Disposition and Reporting of Anomalous Human Research Data."

   * e. JSC-20483, Revision B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

3. APPLICABILITY.

   a. JSC. Applies to all members of investigative teams, including research subjects, in all research and experiments involving human subjects that are funded or sponsored by JSC; conducted in JSC facilities, aircraft, or NASA spacecraft; or which involve JSC to any degree.

   * b. Contracts and Agreements. All human research conducted under contracts, grants, cooperative agreements, and Space Act agreements entered into by JSC and another Government agency, private entity, non-Federal public entity, or foreign entity must comply with this Management Instruction and NMI 7100.8.

4. DEFINITIONS. There are at least two definitions of scientific misconduct. One definition concerns scientific investigators who may be guilty of willful fabrication, falsification of data or records, plagiarism, or some other serious deviation from accepted practice in proposing, implementing, or reporting research. A complementary definition concerns research subjects who willfully and knowingly engage in one or more forms of behavior specifically prohibited in the relevant research proposal or protocol.

5. POLICY.

a. Scientific Investigators. No scientific investigator funded by a NASA grant or contract shall at any time be permitted to engage in scientific misconduct as defined in Paragraph 4. Allegations of such behavior will be considered serious. Procedures for disposing of such allegations are outlined in Paragraph 6a.

b. Research Subjects. No subject will willfully, knowingly, and purposefully engage in any form of behavior specifically interdicted by the investigator in his/her experimental protocol or requirements that would thwart the objectives of the research or result in spurious and/or uninterpretable data.

(1) The interdicted behavior on the part of the subject must be done willfully and knowingly and not be a simple unintentional omission or commission due to forgetfulness or misinterpretation of requirements. In this context, it will be the responsibility of the investigator and/or the Project and Mission Scientists to remind the subjects of permitted and proscribed behavior at repeated intervals, namely, at appropriate times prior to each session of baseline data collection, training exercises, KC-135 flights, etc.

(2) The proscribed types of behavior must be clearly detailed by the Principal Investigator in the document attached to the NASA Informed Consent Statement or form. This description of the experiment must be in nontechnical terms such that a person without a scientific background could clearly understand what will be done to the subject. The document should also clearly indicate what behavior is or is not permitted. Thus, time and types of exercise, hours of sleep, dietary limits, interdicted foods, over-the-counter or prescription medications, and a detailed description of the known medications to be administered to the subject must be provided to include their principal pharmacological actions, undesirable side-effects, idiosyncratic reactions, and any other pertinent information that may be of importance. The risks associated with certain pharmaceuticals (including radionuclides) must be stated insofar as these are known. The importance of this document cannot be overstressed, since it may serve as a basis for crew selection and will serve as the source document in determining whether allegations of subject scientific misconduct may have occurred.

6. PROCEDURES.

* a. Scientific Investigators. Allegations of investigator scientific misconduct shall be treated with the utmost sensitivity and shall be brought to the attention of the Chairperson, JSC Institutional Review Board (IRB).

Depending upon the gravity of the allegations, the IRB may elect to remand the matter to the Office of the Inspector General for substantiation of the allegations, since the IRB has limited investigative authority. If such allegations are verified, appropriate higher NASA management shall be apprised of the facts of the matter and may wish to consider what sanctions may be warranted. At this point, NASA may elect to report the matter to appropriate administrative personnel of the investigator's parent organization. The possible penalties for investigator misconduct are given in Paragraph 7a.

b. Research Subjects. Should scientific misconduct on the part of any subject be suspected or alleged, the problem should be resolved utilizing the initial part of the procedure prescribed for in JMI 7170.3.

7. PENALTIES FOR SCIENTIFIC MISCONDUCT.

a. Penalties for Scientific Investigators. Sanctions or penalties for scientific investigators guilty of scientific misconduct shall be assessed on a case-by-case basis by the appropriate level of NASA management. In the case of JSC employees, they may be subject to appropriate disciplinary actions up to and including dismissal.

Non-JSC investigators and contractor employees may be subject to similar sanctions as deemed appropriate by their respective employer. In addition, NASA may take additional actions severing all relationships with the individual and/or employer, including termination of grants, cooperative agreements, contracts, or Space Act agreements.

b. Penalties for Research Subjects. Research subjects found guilty of scientific misconduct are subject to the same penalties described in Paragraph 7a.

8. DISPOSITION. Ultimate disposition will be on a case-by-case basis with management decision based on an evaluation of the inputs from as many of the elements listed in Paragraph 6 as may be required. Penalties and/or sanctions, if appropriate, will be prescribed or recommended by Center management.

9. RESCISSION. JMI 7071.2, dated July 14, 1994.

Original Signature:
George W. S. Abbey

George W. S. Abbey
Director

DISTRIBUTION: A-3

JOHNSON SPACE CENTER
MANAGEMENT
INSTRUCTION

JMI 1382.5A
Effective Date: December 27, 1995
Expiration Date: Until Rescinded

Responsible Office: SA

Subject: MAINTAINING THE PRIVACY OF BIOMEDICAL RESEARCH DATA

1. PURPOSE. This Management Instruction establishes a policy for protecting the privacy of data collected during voluntary medical research involving active, inactive, or retired space flight crew members and for ground-based and in-flight data collection. This addresses the protection of the privacy of the crew member's data, as well as the protection of NASA's interests for safety of flight by allowing the collection of data necessary for the development of countermeasures to the adverse effects of space flight on human physiology.

2. SCOPE. This Management Instruction applies to medical payload experiments as well as Detailed Supplementary Objectives and includes preflight, in-flight, and postflight data.

3. REFERENCES.

   a. NASA Management Instruction (NMI) 7100.8, "Protection of Human Research Subjects."

   b. NASA 10HERD, "Human Experimental and Research Data Records," Privacy Act of 1974, Systems of Records.

   c. NASA 10HIMS, "Health Information Management," Privacy Act of 1974, Systems of Records.

   * d. JSC Handbook (JHB) 1107.1, "The JSC Organization."

   e. JSC Management Instruction (JMI) 1382.8, "Privacy Act of 1974."

   * f. JSC-20483, Revision B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

4. POLICY. Medical research data shall be handled in accordance with the references in Paragraph 3 and with the additional specific provisions set forth below:

   * a. Each investigator must submit with the research proposal a plan for maintaining the privacy of the data collected. For currently approved investigations, the investigator must submit an updated plan for maintaining the privacy of the data collected to the JSC Institutional Review Board (IRB) for approval prior to the next flight on which the investigation is manifested.

* b. Data may be shared among investigators as specified in each investigator's initial proposal. These plans for data sharing must be approved by the IRB prior to implementation.

c. Data collected during medical research protocols will not be used to determine the aeromedical certification of crew members. Data that indicate a life-threatening condition may, however, require additional medical evaluation necessary for appropriate medical follow-up for the individual and aeromedical certification.

d. Should an abnormality be detected that is life-threatening, the investigator shall provide and/or obtain medical care for the crew member. The Flight Medicine Clinic shall be notified to provide this care.

* e. Preflight, in-flight, and postflight medical research tests will be monitored by the investigator and by a medical monitor as required by the IRB. In-flight data collection will also be monitored by the flight surgeons in the Mission Control Center when the IRB determines that the investigation represents a potential hazard to the crew's health during space flight.

5. BACKGROUND. Data collected during medical research can potentially affect a crew member's career should an abnormality be detected. To protect the confidentiality of the data collected, data will be managed according to the references in Paragraph 3 by all data collection personnel and the investigators of each proposal. General group results may be released, but an individual crew member will not be identified except as noted in Paragraph 4d.

6. RESCISSION. JMI 1382.5, dated March 22, 1994.

Original Signature:
George W. S. Abbey

George W. S. Abbey
Acting Director

DISTRIBUTION: A-3

Policy Guidelines for Space Flight Medical Research and Experiments

Fundamental Ethical Principles

There are fundamental ethical principles for experiments that involve human beings. These include, among others, the following: 1) Experiments are performed only on people who freely volunteer for the experiments, without coercion in any form; 2) A subject may withdraw from an experiment at any time, for any reason; 3) If immediate withdrawal from an experiment causes significant medical risk, the subject will be provided the necessary care by the Principal Investigator's (PI's) institution to allow him/her to withdraw safely and promptly from the experiment.

Crew Flight Assignment

For Spacelab missions with large life sciences components, it is the responsibility of the mission scientist to be sure that the experiments are well defined prior to requesting crew assignment. For other missions, any life science experiments that will be flown as primary or secondary experiments (vs. DSO's) should also be manifested prior to crew assignment. In all cases, risks as well as any medical qualifications (e.g., no patent foramen ovale) should be clearly stated.

Potential crew members will provide informed consent prior to flight assignment. They are to be told about all human experimentation that is to be done, the risk involved, total radiation, pain involved, all pre- and post-baseline data collection, including what studies will be done concurrently. The presentation for payload specialists will be the same as for other crew members. If the exact experiments to be flown are not finalized prior to the need for crew selection, then the proposed crew could provide informed consent to a slightly larger group of experiments that may fly, and the ones that do fly would be a subset of the larger group. If any changes are made to the experiments after the consent is signed, then the crew can refuse the changes without any repercussions.

Conducting and Monitoring Experiments

The PI is responsible for ensuring that experiments are conducted properly and safely, according to the protocol approved by the HRPPC. There shall be a mechanism to monitor the compliance of PI's. This mechanism would help the HRPPC to ensure that protocols are conducted properly, that baseline data collection is performed safely and is limited to only data that are associated with the flight.

In addition, a medical professional(s) shall be identified to monitor the health of the subject during the implementation of protocols designed by the HRPPC as requiring the presence of a medical monitor. These individuals would be responsible to the chairperson of the HRPPC and have no relationship to the research or the researchers.

Risk Reduction

The mission scientist is responsible for thoroughly briefing the crew surgeon on all of the human experiments that are to be conducted on any specific mission. Further, the crew surgeon and mission scientist together are responsible for developing an overall risk

assessment of the protocols, which would then be presented to the Human Research Policy and Procedures Committee (HRPPC) before the flight. The presentation will specifically address risks due to performing several protocols over a short time (e.g., drug interactions). In addition to the individual experiment consent forms, there will be a consent form for the subject to agree to participate in the overall set of timelined experiments. In combining protocols, consideration will be given to the following: total radiation; total blood drawn; equal distribution of subject participation; and appropriate limits on the amounts of time spent being a subject.

The HRPPC

1. Robustness: The membership of the HRPPC should be evenly balanced among disciplines. Also, members of the HRPPC recognize that if, in fact, a protocol were to be approved over their strong objection, they can and should pursue appeal to senior management before such a protocol would be implemented.

   The HRPPC should also consider extending membership to non-NASA government clinicians, such as DOD, VA, and NIH physicians. At least one ethicist could also participate. This person could conceivably be found at a local medical center and hired as a part-time government expert. Studies involving local community members as subjects require that their special needs and/or interests be represented. This non-scientific outside member (the ethicist) may best serve these individuals.

   In addition, individuals with competence in specialized areas should continue to participate and assist the HRPPC as appropriate in review of complex issues. Medical specialists, such as cardiologists, immunologists, or behavioral scientists, may better define risks or available alternative procedures. Such specialists would not necessarily vote with the HRPPC.

2. Conflict of interest: It is essential that the members of the HRPPC be free from any conflict of interest in regard to protocols they review. The governing regulations require that any conflict of interest in regard to protocols they review. The governing regulations require that any HRPPC member who is a PI, co-investigator, or supervisor of the investigator(s) of a protocol before the HRPPC not participate in the HRPPC's vote on that protocol. The HRPPC must be sensitive to any potential conflict of interest.

3. Interactive risks among experiments: The HRPPC should design a more formal process to evaluate interactive risks among experiments.

   a) Combined protocols for space flight produce situations not encountered in typical clinical experiments where time and procedure constraints are usually less severe than in a space flight environment. Limited experience with combining protocols with these constraints makes assessment of overall interactive risk difficult. Nevertheless, a formal process to assess and minimize interactive risk, with input from all PI's, should be established.

b) The mission scientist and crew surgeon are required to conduct an evaluation of interactive risks to astronaut test subjects for composite experiments on each flight, including the order and sequence of experiments for each participant. Potential hazards should not be limited to interactive pharmacologic risks, but should also include assessment of medical experimental hardware on crew performance or emergency egress. Attention should be directed toward the combined physiologic or psychologic impact of all procedures on the subject. The mission scientist and the crew surgeon will present the interactive risk profile for consideration by the HRPPC.

c) The HRPPC must incorporate interactive risks to the test subject as part of informed consent. Conceptually, all drugs and procedures need to be reviewed for adverse interaction or synergistic risk probability.

4) Autonomy and Impartiality of the HRPPC: An impartial HRPPC is essential to life sciences at NASA. There must never be influences exerted by anyone to replace individual members of the committee in order to reduce the viewpoints presented. Individual members must feel free to express opinions and concerns without fear of career repercussions.

Privacy of Experiment Data and Medical Records

Consent forms that exist cannot be violated. The baseline consent forms should only provide for data distribution to the most limited data bases. However, subjects can be asked to voluntarily provide their data to data bases with various levels of distribution. The voluntary request can be done before and/or after the experiment, showing the subject exactly what is proposed for release and what level of release is proposed.

No data will be publicly released that can be attributed to an individual except as provided in the previous paragraph. This encompasses not only absence of the individual's name, but also requires sufficient pooling of data so that the individual's identity cannot be determined by combining or cross-referencing data (e.g., height, weight, sex, and flight number may identify a specific individual).

Separate from the scientific data bases, there is a need for a data base of adverse reactions that is available to appropriate PI's, potential subjects, and medical monitors so they can be aware of previous experiences with specific protocols. Consent forms should specifically describe previous adverse reactions experienced during NASA-sponsored tests of the protocol or similar protocols.

The Health Information Management System (HIMS) and Human Experimental and Research Data Records (HERD) data bases already contain all currently collected data. From these data bases additional ones could be created that contain the following: 1) data to be made available on a need-to-know basis; 2) data documenting adverse reactions to protocols during NASA testing. These data would be available to fight surgeons, principal investigators, and potential subjects to help provide informed consent and to be prepared if a similar adverse reaction occurs.

An oversight board with representatives from life sciences, flight surgeons, and the Astronaut Office is needed for configuration and control of the data bases.

There should be a postflight debriefing with the flight surgeons, investigators, and crew members where the experiments and the crew's reactions are discussed in detail and the discussion is protected as private medical data; for long duration flights, periodic discussions can be conducted during the flight.

Coercion

No one can be forced to participate or continue participation in an experiment. Coercion to participate can take many forms and must be vigilantly avoided. There shall be no agreements that imply consent prior to being informed of the detailed risks of the experiment.

Withdrawal from Experiments

The crew member and the PI should try to wor problems themselves. If this is not possible, then the possibility should exist fo the experiment and/or the crew member to be removed from the flight. This bility will provide motivation to both sides to work out an agreement. The mechan f resolving disagreements betwee crew and investigators needs to be specifically mined. We support the procedures specified in the proposed revisions to NMI 7100. egarding withdrawal from flight.

Results

When a protocol is proposed for reflight, the results and significance of previous data should be presented to the Scientific Merit Review Committee (SMRC). The total number of subjects needed to complete the study should be estimated up-front (e.g., with a power analysis). Any increases in that number would have to be justified.

Flight Surgeon/Astronaut Relationship

A flight surgeon must be able to use his or her judgment in protecting patients' privacy. Strict guidelines regarding when to report medical problems are difficult to determine. Some reasonable principles include the following: 1) Medical problems revealed during an in-flight private medical conference should be shared with the other physicians serving as mission controllers during that mission and with the Chief of the Medical Operations Branch; 2) The problems can be shared with other flight surgeons who are assigned to the flight control team when appropriate; e.g., to obtain the opinion of a more experienced flight surgeon; 3) If a medical event occurs that may have potential mission impact, then medical management needs to be thoroughly briefed; therefore, for medical problems with potential mission impact, the Chief of the Medical Operations Branch will brief the Chief of the Medical Sciences Division. For medical problems with a determined mission impact, non-medical management will be briefed only on those clinical details required to assess mission impacts and a limited public statement will be released according to JSC Management Directive 3610.3B.

Responsibility and Accountability

The PI is responsible for conducting experiments safely and in accord with the protocol approved by the HRPPC. The HRPPC is the responsible body for certifying that experiments conform to the guidelines regarding human subjects. The Chairman and the members of the HRPPC review all human protocols and ensure that each protocol, as well any integrated set of protocols, are safe. The Chairman of the HRPPC informs Principal Investigators of the PI's responsibility to strictly follow approved protocols. The HRPPC also takes appropriate action when PI's fail to follow protocols. The HRPPC should establish a mechanism to assure that protocols are followed and deal with any discrepancies.

Line management has the responsibility to determine that the protocols conducted by PI's are needed by NASA, approved by the HRPPC, that pretest reviews are conducted, and that all participating experiments, staff, and subjects know their roles and responsibilities. Line management also has the responsibility to actively assure that protocols are performed carefully and are strictly followed according to HRPPC guidelines, and that the people involved in conducting experiments are properly qualified. They are also responsible to assure that actions brought by the HRPPC are followed in the work unit, including follow through on adverse actions directed by the HRPPC.

Concurrence:

Original Signature:
David C. Leestma, 3/8/95

David C. Leestma
Director, Flight Crew Operations

Original Signature:
Donald E. Robbins, 3/8/95

Donald E. Robbins
Acting Director, Space & Life Sciences

Guidelines for Test Readiness Review

(Reprinted from JHB 1700.1 - *JSC Requirements Handbook for Safety, Health, Environmental Protection, and Emergency Preparedness*, Section II, Chapter 21, Part 8, Number 3.)

3. GENERAL TEST PROCESS

This process, with the exception of paragraph 21.8.3.a below, does not generally apply to nonhazardous test as defined above. However, with nonhazardous tests, prepared test documentation shall be made available to NS3 upon request. The testing organization and NS3 may decide to incorporate some elements of this process for a "nonhazardous" specific test. The testing organization and NS3 may decide that some elements are not necessary for a specific "hazardous" test after evaluation of the hazard level involved. The detailed test process for each testing organization is found in its operating procedures.

a. Safety Notification Testing organizations shall notify NS3 of upcoming test operations by test request, schedule, or equivalent means.

b. Test Documentation

The following documentation shall be completed prior to the test.

(1) The test is a top level first glance at the test. A test plan shall be written for each new test. The test plan shall include as a minimum:

(a) Test objectives

(b) Safety and medical planning provisions and known medical issues

(c) Test requirements

(d) Special safety considerations for test

(e) The test plan may include other items if required by the testing organization.

(f) Test plans containing final detailed test procedures (as described below) shall be approved in the same manner as a detailed test procedures document.

(2) The detailed test procedures (DTP's) describe the steps by which the test will be run. Test procedures should be available for critical review a minimum of 3 to 5 days prior to start of the test. Test procedures shall be written in a step-by-step sequential format. Procedures shall be written to ensure that appropriate measures are specified to prevent mishap/incidents from occurring. DTP's shall include the following as a minimum:

(a) Operating procedures to accomplish the test

(b) Emergency procedures which describe actions to be taken in the event of systems failure or malfunction

(c) Test rules which define equipment and instrumentation limits, operating limits, off-nominal conditions, and operational situations which would require abort, hold, or proceed decisions for each test or checkout operation

(d) The safety requirements, individual tasks, and personnel involved in hazardous operations

(e) Special considerations and procedural steps that address specific hazards identified during the hazard analysis process. These and steps containing actions critical to the protection of life and/or property shall be flagged as safety critical steps for easy identification by test team personnel.

(3) Each DTP that contains safety critical steps shall contain a statement to that effect on its cover.

(4) Emergency procedures shall be immediately available to test personnel at their duty stations unless circumstances prohibit (i.e., divers).

(5) The testing organization shall provide a process for concurrence on DTP's by NS3.

c. Safety Assessment

(1) Test systems and operations shall undergo a safety assessment by a process which identifies the hazards associated with the test, their controls, and verification of their controls. The process shall be outlined in the testing organization's operating procedures, which shall identify specific assessment subjects. The process should begin in the early phases of test planning and operations and should involve NS3 at every step. All hazards shall be controlled and closed prior to the test.

(2) The results of the safety assessment shall be documented as provided for in the testing organization's operating procedures. Existing safety assessments only need be updated to reflect analysis of changes to the hardware or operations for repeat tests.

(3) Section I, Chapter 1[illegible] System Safety and Risk Assessment", of this manual describes sy[illegible]n safety requirements and concepts. JSC 17773, "Instructions for Preparation of Hazard Analysis for JSC Ground Operations", (current version) may be used as a guideline for format or thought process for conducting safety assessments. Other references

include: MIL-STD-882, "System Safety Program Requirements", and NHB 1700.1, Volume 3, "System Safety."

d. Test Readiness Review

(1) A test readiness review (TRR) shall be held for each test or series of tests. This review shall determine the readiness of the test facility and article: adequate completion of the safety assessments; status and closure of key issues, constraints, and open items; and qualification/certification of the test team.

(2) The Test Readiness Review Board (TRRB) will be chaired by a management official or designee from the testing organization who is not personally involved with the test. Its membership will include as a minimum: an NS3 representative; a Medical Operations Branch representative (if appropriate); and the Quality Assurance and Engineering Division (mail code ND) (for tests supported by ND). The TRRB members will sign a readiness statement to indicate approval for the test to proceed. Signatures will indicate as a minimum that the test configuration, staffing, operation, procedures, and safety assessments are approved.

e. Pretest Briefing A pretest briefing conducted by the TD or TC shall be held for each series of tests. The intent is to ensure that all test team members understand the normal and emergency operational aspects of the test.

f. Pretest checkout Pretest checkout operations, using approved test procedures, shall be conducted prior to each series of tests to assure that the test personnel will function effectively as a team and that the facility and test equipment are compatible. The pretest checkout operations shall include

(1) Verification that all critical systems are functional

(2) A "dry run", if feasible, for complex tests. The intent is to exercise the facility and equipment for final compatibility and provide training and familiarization for the test team.

(3) Simulated emergency drills peculiar to the specific test team.

g. Posttest Debriefing A posttest debriefing conducted by the TC or TD should be held for manned and complex tests. The intent is to discuss the test results and any facility or test system anomalies that have occurred with the test team.

h. Posttest Documentation

(1) Test Report. A test report, if prepared, should include safety lessons learned and be made available to NS3.

(2) Mishap Reports. Mishap reports are required for any incident causing damage or injury or any incident with the potential to cause damage or injury (close call). Refer to JSCMD 1710.14, "Mishap Reporting, Investigating, and Corrective Action" (current version) and Section I, chapter 4 of this manual for policy, criteria, and format for mishap reporting.

i. Repeat Testing Tests utilizing previously approved configurations and procedures may be repeated without another TRR, as long as the test complies with the constraints of the original TRR and the paperwork has not changed. Modifications to the hardware or procedures will require a new TRR. Modified procedures and safety analyses shall be approved in accordance with the testing organization's operating procedures.

j. Real Time and Quick-Turnaround Testing Refers to testing that is required real time to support a mission or permission testing required to support a space mission. This is defined as testing that is essential for timely start or safe continuation of the mission. For this type of testing, the test procedures shall be prepared and approved and a TRR held. NS3 shall be notified of such tests as soon as possible. An NS3 representative shall be present for any procedure reviews, the TRR, and the test, if required by paragraph 21.7.1c(3) of this chapter.

Appendix S

Examples of Approved Medical Monitoring Practices

A. EXERCISE LABORATORY

Exercise stress testing involving flight crew subjects will be constrained within the following guideline:

1. Exercise target heart rates and/or oxygen consumption levels will be sub-maximal with the objective end point not to exceed 85% of preflight maximum levels during all in-flight and postflight testing immediate postflight (R+0 to R+2) testing. If this guideline is followed, there is no in-flight requirement for electrocardiogram monitoring; heart rate obtained by a "heart watch" and monitored by digital display is adequate.

2. Maximal aerobic exercise tests (treadmill or cycle): "Level 1."

3. Sub-maximal aerobic exercise tests: "Level 2" (for crew or otherwise), except when testing is occurring between landing day and R+3 (or post-bedrest days 1-3 for test subjects), when testing will be designated as "Level 1."

4. Muscular resistance tests: "Level 4" except for astronauts during postflight period ("Level 3").

B. CARDIOVASCULAR LABORATORY

1. Presyncopal LBNP tests: "Level 1."

2. Ramp (non-presyncopal) LBNP tests: All initial and all postflight LBNP ramp tests (the latter up to R + 3) will be designated "Level 1." All non-initial preflight (and pre-bedrest) ramp tests, as well as ramp tests which follow an initial "Level 1" presyncopal test, will be "Level 2" unless the supervising civil servant physician (see prior notes) recommends that they be treated as "Level 1", in which case testing will not proceed unless and until appropriate "Level 1" personnel become available. All in-house LBNP tests will employ a Finapres device to maximize safety.

3. Stand or tilt tests

   a. For post-bedrest subjects, tilt tests will be designated "Level 1", and stand tests will be designated "Level 2."

   b. For ambulatory subjects, tilt tests will be designated "Level 2", and stand tests will be designated "Level 3."

4. Infusions: Always "Level 1" for drugs/medications, especially substances influencing blood pressure, heart rate, or heart rhythms.

5. Carotid barocuff testing: "Level 2."

6. Vasalva testing: "Level 2."

7. Fluid loading studies (i.e., administration of salt tablets, Florinef, or Arginine Vasopressin for plasma volume or tolerance determinations): "Level 3."

C. ENVIRONMENTAL LABORATORY

1. LES/LCG tests: "Level 2."

2. Cold pressor/cold exposure tests (not at vacuum): "Level 2."

3. BENDS Testing: Handled as "Level 1" by SD2 physicians.

D. NEUROSCIENCE LABORATORY

1. All testing designated as "Level 3."

E. OTHER TESTING

1. New studies employing procedures other than those mentioned above (i.e., new procedures, infusions of nonvasoactive drugs, dyes, etc.): Monitoring level to be assigned by the Board on a case-by-case basis.

2. The medical studies of outside investigators centered around special shuttle flights (i.e., D-2, SLS-2): Medical monitoring levels/responsibilities to be designated and assigned by the Board to the most appropriate medical personnel (i.e., SD2 or SD4/5 physicians plus/minus mission-affiliated non-civil service medical personnel) in advance of preflight medical testing.

JOHNSON SPACE CENTER
POLICY
DIRECTIVE

JPD 7170.3A
EFFECTIVE DATE: May 13, 1996
EXPIRATION DATE: Valid Until Rescinded

Responsible Office: SA/Space and Life Sciences

Subject: DISPOSITION AND REPORTING OF ANOMALOUS HUMAN RESEARCH DATA

1. PURPOSE. To define the policy and implementation procedures for reporting, resolving, and disposing of anomalous human research data.

2. REFERENCES.

   a. NASA Management Instruction (NMI) 7100.8, "Protection of Human Research Subjects."

   b. NMI 8900.1, "Medical Operations Responsibilities and Human Space Flight Programs."

   c. NASA 10HERD, "Human Experimental and Research Data Records," Privacy Act of 1974, System of Records.

   d. NASA 10HIMS, "Health Information Management," Privacy Act of 1974, System of Records.

   *e. JSC Handbook (JHB) 1107.1, "The JSC Organization."

   f. JSC Management Instruction (JMI) 1382.5, "Maintaining the Privacy of Biomedical Research Data."

   g. JMI 1382.8, "Privacy Act of 1974."

   h. JMI 7170.1, "Withdrawal of Flight Crew Subjects from Human Research."

   i. JMI 7170.2, "Scientific Misconduct with Regard to Human Research."

   *j. JSC-20483, Revision B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

3. APPLICABILITY.

   a. JSC. Applies to all members of investigative teams in all research and experiments involving human subjects that are funded or sponsored by JSC; conducted in JSC facilities, aircraft, or NASA spacecraft; or which involve JSC to any degree.

b. Contracts and Agreements. All human research conducted under contracts, grants, cooperative agreements, and Space Act agreements entered into by JSC and another Government agency, private entity, non-Federal public entity, or foreign entity must comply with this Policy Directive and NMI 7100.8.

c. Mission Management. Applies to Mission and Science Managers as defined below.

4. DEFINITIONS.

a. Anomalous Data. Experimental data lying outside the expected norm for the healthy general population cohort or for a particular subject.

b. Mission Manager. The NASA employee responsible for the overall development, integration, and operation of the mission payload.

c. Mission Scientist. The NASA employee responsible for the scientific conduct of the mission.

d. NASA Astronaut. A career NASA astronaut assigned as a commander, pilot, or mission specialist on a particular mission.

e. Payload Specialist. A non-career astronaut possessing unique skills required for a particular mission and selected by the Investigator Working Group to participate as human experimental subject/operator on that mission.

f. Principal Investigator (PI). A scientist whose proposed flight experiment has been selected for a specific mission.

g. International Mission Specialist. A career international astronaut assigned payload duties on a particular mission.

h. Project Scientist. The NASA field Center scientist/manager responsible for the detailed development of flight experiments, representing the interests of selected investigators, and for interfacing their experiments with the various mission organizations.

i. Senior Life Sciences Management. In the context of this Policy Directive, consists of the Director, Space and Life Sciences; the Life Sciences Project Scientist; and the Headquarters Director of Life Sciences.

j. Designated Medical Officer (DMO). The individual responsible for recommending the final medical disposition on all medical issues. When required, expert ad hoc committees or consultants may be utilized by the DMO in the discharge of this responsibility. Normally, in the context of this Policy Directive, the DMO will act alone on issues submitted for resolution.

*5. BACKGROUND.

*a. The possibility exists that a crew member dedicated to a space flight mission may exhibit preflight test data which may be considered abnormal for that individual or out of the established norms for a group of individuals of the same gender and age bracket. If unique physiological mission requirements exist for an experiment or set of experiments, screening of potential applicants will be done prior to selection. In this way, if an individual's "normal" state is outside mission limits, this will preclude the selection of unsuitable candidates.

b. The procedures set forth in JMI 1382.5 and supporting applicable references provide guidelines for reporting potentially life-threatening data. This Policy Directive establishes procedures relating to the situation in which experimental data are determined not to be life-threatening, but may nonetheless have serious scientific implications or impact on the human experiments payload and mission success.

6. PROCEDURES. The following steps are designed to accomplish the expeditious disposition of anomalous data while maintaining the privacy of the individual involved. The procedure is designed first to assure the health and well-being of the subject from whom the anomalous data was collected, and second, to maintain the scientific integrity and success of the mission. The procedures outlined in this Policy Directive need not be pursued in their entirety. The process sequence may be terminated at that point at which the PI is satisfied that a reasonable and acceptable explanation of the cause of the anomalous data has been found and that the individual is acceptable as a subject for the experiment(s) in question. The process is divided into 10 major sequential phases. In order to assure orderliness and efficiency, maximum time periods are allotted for each of these phases. All participants should attempt to complete these priority actions within the indicated time frame.

NOTE: At each phase of the following process, the identity of the subject will be divulged only to those individuals with a need to know, in order for them to make the necessary assessments regarding scientific impacts. In each of the following steps, when written reports are submitted, the research subject shall receive a copy.

*a. Detection (1 week). When an investigator completes a preflight data collection protocol and has sufficiently reduced the data to be confident that the data are not in error in any manner known to the investigator, it is necessary for the investigator to identify any data which are anomalous. The investigator should immediately discuss the anomalous data with the subject and jointly attempt to resolve any potential cause(s) for the anomaly or come to an agreement about future participation in this experiment. The investigator and subject should repeat any test(s) when this is feasible and when such repetitions might lead to an explanation or elimination of the anomalous data.

*b. Reporting anomalous data to the Project Scientist (3 days). If the investigator and subject are not able to resolve the cause of the anomalous data or agree upon future participation, the investigator shall provide a written summary of the findings to the Project Scientist responsible for the experiment. The Project Scientist may request additional information from the investigator and/or other medical consultants in order to assist in determining the source or cause of the anomalous data or agree upon future participation. The subject may likewise seek additional medical opinions as appropriate.

c. Reporting anomalous data to the Mission Scientist (2 days). If the Project Scientist is unable to determine a satisfactory explanation for the anomalous data, a written summary of all findings will be provided to the Mission Scientist. Along with the specific findings, the Project Scientist will provide to the Mission Scientist any preliminary indications of potential impact(s) these data may have on other investigations on the mission.

*d. Immediate reporting of anomalous data to the Designated Medical Officer (DMO).

*(1) To assure that the data in question are not life-threatening, the Mission Scientist will verbally communicate the information reported by the Project Scientist to the DMO. The Mission Scientist and/or the DMO, at this time, may also contact the PI and/or subject for any clarification. All of the above reports will also be summarized in writing for the record. Life-threatening findings by an investigator are covered in detail in JMI 1382.5.

*(2) If it is determined, in writing, by the DMO that the anomalous data are not potentially life-threatening, the Mission Scientist will contact the Project Scientist and approve the notification of all potentially affected PI's. Should the DMO determine that the data indicate a potentially life-threatening situation, the standard procedures in place for such an eventuality take precedence and the remaining procedures for determining scientific impact as described in this Policy Directive may be terminated.

*e. Determining overall impact of anomalous data on scientific conduct of the mission (1 week). The Project Scientist, after approval from the Mission Scientist, will inform each potentially affected PI in writing of the findings to date. As noted previously, the Project Scientist must determine whether the identity of the subject is required for the investigators to make their evaluation and the former must advise the subject if this is necessary. Each PI should provide a written statement (with supporting evidence) regarding the manner in which the anomalous data may or may not impact the scientific results of his/her experiment. The Project Scientist will provide an integrated assessment (in writing) to the Mission Scientist of all findings regarding the anomalous data.

f. Development of mission science recommendations (1 week). After the Mission Scientist has received input from the Project Scientist regarding the impact on individual investigations, the Mission Scientist will review and develop a written mission science recommendation which includes an assessment of all mission elements. If the assessment of the Mission Scientist is that there is no mission impact, then the process is terminated at this point. If, however, the assessment is that there is a mission impact, then the process continues as follows.

g. Anomalous data caused by prohibited behavior. Willful, knowing, and purposeful behavior on the part of a research subject that is specifically prohibited by an investigator in his/her experimental protocol or requirements and that results in anomalous human research data shall be considered scientific misconduct and shall be dealt with as specified in JMI 7170.2.

h. Providing knowledge of anomalous data to the Mission Manager or equivalent, and/or the Director, Flight Crew Operations (2 days).

*(1) If the crew member is a Payload Specialist, the written mission science recommendation shall be provided to the Mission Manager or equivalent (with copies to JSC Life Sciences senior management; the Legal Office; the Director, Flight Crew Operations; the Chief, Astronaut Office; and the Mission Commander).

*(2) If the crew member is a NASA astronaut or international mission specialist, the Mission Scientist shall provide the written mission science recommendation to the Director, Flight Crew Operations (with copies to the Director, JSC Space and Life Sciences; the Headquarters Director, Life and Biomedical Sciences and Applications Division; the Legal Office; the Chief, Astronaut Office; the Mission Commander; and the Mission Manager or equivalent).

*i. Mission impact statement (1 week). The Mission Manager or equivalent shall provide a mission impact statement to the Director, Flight Crew Operations; the Director, JSC Space and Life Sciences; the Headquarters Director, Life and Biomedical Sciences and Applications Division; the Legal Office; the Chief, Astronaut Office; the Mission Commander; and the Mission Scientist.

*j. Possible reassignment of crew members.

*(1) Should a renegotiation of the availability of NASA astronauts or international mission specialists be required in order to support the mission, JSC Life Sciences senior management and the Director, Flight Crew Operations, will develop a mutually agreeable position. The subject will be allowed to make inputs to this forum if he/she desires. The Director, Flight Crew

Operations, makes the final decision regarding NASA astronaut and international mission specialist assignments. If only a NASA astronaut or international mission specialist is involved, at the end of satisfactory negotiations regarding availability, the procedures outlined in this Policy Directive are terminated.

*(2) When the crew member involved is a Payload Specialist, the Mission Manager or equivalent will support the development of a joint statement/recommendation to be provided to the appropriate Headquarters Associate Administrator. Inputs from the Mission Scientist; JSC Life Sciences senior management; Director, Flight Crew Operations; the Legal Office; the Chief, Astronaut Office; the Mission Commander, and the subject shall be included when those inputs are deemed necessary in assisting the appropriate Headquarters Associate Administrator either to accept or reject the joint recommendation.

k. Center Director decision. The final step is the decision of the Center Director, acting in consultation with the appropriate Headquarters Associate Administrator based on the joint recommendation of the involved parties regarding the anomalous data and its scientific and operational impact on the mission. This decision may or may not result in the removal and/or reassignment of crew members to the mission.

7. RESCISSION. JMI 7170.3, dated July 14, 1994.

*Denotes change.

Original Signature:
George W. S. Abbey

George W. S. Abbey
Director

DISTRIBUTION:
A-3
NODIS

NASA
National Aeronautics and Space Administration

NASA Mishap Report

MASTER FILE NO.

NOTE: Fill in unshaded blocks within 24 hours. Please print or type. See reverse for instructions.

GENERAL INFORMATION

1. NAME OF ORGANIZATION	2. MISHAP DATE (*MDY*)	3. MISHAP TIME (*24 hrs.*)	4. ORG. FILE NO.

5. MISHAP CATEGORY (*CHECK AS APPROPRIATE*)

TYPE A	TYPE B	TYPE C	INCIDENT
1 [ ] DEATH	2 [ ] LOST TIME	2 [ ] LOST TIME	4 [ ] INJURY
2 [ ] LOST TIME	3 [ ] PERM. DISABILITY	4 [ ] INJURY	6 [ ] DAMAGE
4 [ ] INJURY	4 [ ] INJURY	6 [ ] DAMAGE	MISSION FAILURE
6 [ ] DAMAGE	5 [ ] HOSPITALIZATION	7 [ ] TEST FAILURE	[ ]
7 [ ] TEST FAILURE	6 [ ] DAMAGE		
	7 [ ] TEST FAILURE		

6. CLOSE CALL [ ]	7. LEVEL OF POTENTIAL	8. BLDG. NO./LOCATION

9. SPECIFIC AREA

10. MISSION AFFECTED	11. PROGRAM IMPACT

12. DESCRIPTION OF MISHAP (*Sequence of events, extent of damage and injuries, cause, if known, etc. Use additional sheets if necessary*)

PERSONNEL INVOLVED

13. NAME (*Last, first, middle initial*)	14. AGE	15. SEX [ ] M [ ] F	16. ORGANIZATION (CODE)/POSITION

17. SHIFT WORKED [ ] 1 [ ] 2 [ ] 3	18. HOURS OF CONTINUOUS DUTY BEFORE MISHAP	19. FIRST AID ONLY [ ] YES [ ] NO	20. FATALITY [ ] YES [ ] NO	21. INJURY TYPE (*Code*)

22. BODY PART(S) AFFECTED (*Codes*)	23. DAYS LOST NO.	23. DAYS LOST [ ] TOTAL [ ] CONTINUING	24. CAUSE(S) OF INJURY (*Codes*) PRIMARY	CONTRIB.	POTENTIAL	25. MISHAP ENVIRONMENT (*Codes*) AGENCY	ACTIVITY

26. HAS EMPLOYEE RECEIVED TRAINING/CERTIFICATION APPLICABLE TO TASK? [ ] Yes [ ] No

EQUIPMENT/PROPERTY DAMAGED

27. CLASS OF EQUIPMENT/PROPERTY DAMAGED
1 [ ] FLIGHT HARDWARE
2 [ ] GROUND SUPPORT EQUIPMENT (GSE)
3 [ ] FACILITY
4 [ ] PRESSURE VESSEL
5 [ ] MOTOR VEHICLE
6 [ ] AIRCRAFT
7 [ ] OTHER

28. SPECIFIC ITEM DAMAGED

29. SERIAL/NEMS NO.	30. SYSTEM/SUBSYSTEM AFFECTED	31. CAUSE(S) OF DAMAGE (*Codes*) PRIMARY	CONTRIB.	POTENTIAL	32. COST ESTIMATE $	FINAL $

33. SUBMITTED BY (*Name, title, mail code*)	SIGNATURE	PHONE NO.	DATE

CORRECTIVE ACTION

34. ACTION PLAN (*Provide estimated completion date for each action. Use extra sheets if necessary*)

35. APPROVED (*Name, title, mail code*)	SIGNATURE	PHONE NO.	DATE

36. NASA SAFETY CONCURRENCE WITH CORRECTIVE ACTION PLAN (*Branch chief or higher*)

CONCUR (*Name, title, mail code*)	SIGNATURE	PHONE NO.	DATE

NASA SAFETY OFFICE USE ONLY

37. LESSONS LEARNED [ ] YES [ ] NO	REF. NO. (*If yes*)	40. APPROVAL FOR CLOSURE NAME AND TITLE	PHONE NUMBER
38. TYPE OF INVESTIGATION 1 [ ] BOARD 2 [ ] TEAM 3 [ ] INVESTIGATOR			
39. STATUS		SIGNATURE	DATE

NASA Form 1627 (Jan 89 PREVIOUS EDITIONS ARE OBSOLETE.)

JOHNSON SPACE CENTER
POLICY
DIRECTIVE

JPD 7170.1A
EFFECTIVE DATE: May 13, 1996
EXPIRATION DATE: Valid Until Rescinded

Responsible Office: SA/Space and Life Sciences

Subject: WITHDRAWAL OF FLIGHT CREW SUBJECTS FROM HUMAN RESEARCH

1. PURPOSE. To define the right of NASA to replace any astronaut who withdraws for any reason from any human experiments previously defined as central or core to a Spacelab mission.

2. REFERENCES.

   a. NASA Management Instruction (NMI) 7100.8, "Protection of Human Research Subjects."

   *b. JSC Handbook (JHB) 1107.1, "The JSC Organization."

   c. JMI 1382.5, "Maintaining the Privacy of Biomedical Research Data."

   d. JMI 7170.2, "Scientific Misconduct With Regard to Human Research."

   e. JPD 7170.3, "Disposition and Reporting of Anomalous Human Research Data."

   *f. JSC-20483, Revision B, "JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

3. APPLICABILITY. Applies to human life sciences experiments and includes preflight, in-flight, and postflight phases of the experiment. Further, it applies only to those experiments defined as central to a Spacelab mission BEFORE any NASA astronauts, international mission specialists, or payload specialists are assigned to the space flight in question. This Policy Directive does NOT apply to Detailed Supplementary Objectives or to KC-135 flights.

4. POLICY.

   a. It is the right of NASA management to remove any crew member from any flight when it judges such action appropriate. It is, however, incumbent upon management to inform the crew member of the exact details of the human experiments, in non-technical terms, including the individual experimental protocols and an assessment of all associated risks. This must be done before the astronaut or international mission specialist is assigned to the flight and before the payload specialist is contractually bound to participate in the human experiments of the mission. In consenting to participate in the experiment(s), the crew

members acknowledge the right of NASA management to replace any astronaut who decides not to participate at a later date.

b. Should NASA decide not to replace the crew member, it shall be a matter of policy that the crew member's decision be respected, and that there be no prejudice or harassment expressed or implied by others associated with the mission. It must be further understood that, as a matter of policy, crew member withdrawal from participation in human experiment(s) does not and will not automatically disqualify him or her from future mission assignments. The crew member's withdrawal and the reasons/circumstances for this action, however, may be taken into consideration for future assignments to missions manifesting identical or similar experiments.

*5. CONSEQUENCES OF WITHDRAWAL. Removal from the flight and prejudice regarding assignment to future flights of a similar nature will not be considered if, in the opinion of the JSC Institutional Review Board (IRB), either:

a. the experiment or protocol changed substantially from the original research proposed and agreed to by the crew member, or

b. new valid scientific/medical information has surfaced indicating that the protocol presents an increased health or safety risk above that originally agreed to, or

c. other less hazardous experimental methods are available in reasonable time to support the flight.

Withdrawal for reasons other than those stated in Paragraphs 5a, b, or c could result in removal from the current mission if such action is in the best interest of the flight and the Government and may prejudice the crew member's assignment to missions of a similar nature in the future.

*6. PROCEDURE.

*a. Should a crew member elect to withdraw from participation in human research manifested for a Spacelab mission, the problem should be surfaced as soon as practicable and attempts made to resolve the problem. Specifically, the investigator and the subject should attempt to resolve the problem. Failing this, the Project or Mission Scientist shall assist in arriving at a satisfactory solution. Should these approaches be unsuccessful, JSC Life Sciences senior management and the JSC IRB, with expert consultation as required, will assess the circumstances and forward a recommendation to the Director, Space and Life Sciences; the Director, Flight Crew Operations; the Chief, Astronaut Office; and the Legal Office who will in turn arrive at a consensus decision to be recommended to the Center Director.

*b. The final step is the decision of the Center Director, acting in consultation with the appropriate Headquarters Associate Administrator, following evaluation of as many technical and management inputs as may be required. This decision may or may not result in the removal and/or reassignment of crew members to the mission.

*7. DISPOSITION. In the case of NASA astronauts or international mission specialists, final disposition of the matter will rest with NASA JSC management. For payload specialists, final disposition will rest with the appropriate Headquarters Associate Administrator, acting in consultation with the Center Director.

8. RESCISSION. JMI 7170.1, dated July 14, 1994.

*Denotes changes.

Original Signature:
George W. S. Abbey

George W. S. Abbey
Director

DISTRIBUTION:
A-3
NODIS

Guidelines Relative to Use of Experimental Animals During Preflight Crew Training Activities

These guidelines specifically address the training activities at the home institutions, e.g., medical centers/universities, of the Principal Investigator conducting experiment-specific training and similar training activities at pertinent NASA facilities. Guidelines relative to animal standards and procedures for training simulations utilizing the flight Research Animal Holding Facility (RAHF), chamber simulations (closed environments), and actual space flight are addressed in Appendix X.

All animal holding facilities and/or breeding colonies will generally adhere to the guidelines and recommendations of the Guide for Care and Use of Laboratory Animals, NIH Pub. No. 86-23, and the American Association for Accreditation of Laboratory Animal Care (AAALAC).

Rats

A. The NASA Flight Quality (NFQ) criteria for rats are given in Table 1. In addition to certification that their animals are free of these pathogens, commercial vendors must supply a current health status report for the specific room where the animals selected for the investigation were raised. This report must indicate that the animals are completely free of any known or suspected pathogenic microorganisms or parasites using currently accepted screening technology for murine pathogens. Periodic inspection of the animals for clinical signs of illness by animal handlers is required. Should animals become clinically ill, they will be excluded from the colony and all reasonable attempts made to establish an etiologic diagnosis. In these circumstances, the remaining animals will be recertified pathogen-free, or, alternatively, a new supply secured from the vendor.

B. For training with rats at the above facilities, acceptable laboratory attire is recommended. Ordinarily, this means only a laboratory coat. The use of surgical masks and gloves is crew optional.

Monkeys

NFQ certification will be valid for a period of 6 months. Should hands-on training with monkeys be required at any of the above facilities, the NFQ criteria for space flight animals shall apply (Appendix X). Attire appropriate for personnel protection will be worn by all individuals who have direct contact with nonhuman primates (lab coat, mask, gloves).

Amphibians

The risk of amphibian zoonosis is minimal. Frogs and other amphibians have the potential to carry Salmonella. Acceptable laboratory attire is recommended, viz., a laboratory coat. Other protective measures are crew optional.

Other Species

Other animal species will be considered by the JSC IRB on an individual basis.

TABLE 1. NFQ CRITERIA FOR RATS

MICROORGANISMS	VERIFICATION PROCEDURES
BACTERIA:	
Streptobacillus moniliformis	Oral Culture
Streptococcus pyogenes	Oral and Nasal Cultures
Salmonella sp.	Fecal Culture
Leptospira sp.	Urine Culture
Campylobacter sp.	Fecal Culture
VIRUSES:	
Lymphocytic choriomeningitis virus	Serology
FUNGI:	
Microsporum sp.	Skin (Clinical Inspection)
Trichophyton mentagrophytes	Skin (Clinical Inspection)
ENDOPARASITES:	
Hymenolepis nana	Fecal, Caecal Contents (Microscopic Examination)

Guidelines Relative to Use of Experimental Animals During Crew Training Simulations Utilizing the Flight Research Animal Holding Facility (RAHF) and General Purpose Work Station (GPWS), Chamber Simulations (Closed Environments), and Actual Space Flight

This guideline summarizes the JSC Institutional Review Board's (IRB) current requirements and recommendations regarding subject experimental animal standards and procedures as viewed in the context of past advisory group meetings on this and related topics.

1. All animal holding facilities and/or breeding colonies will generally adhere to the guidelines and recommendations of the Guide for Care and Use of Laboratory Animals, NIH Pub. No. 86-23, and the American Association for Accreditation of Laboratory Animal Care (AAALAC).

2. Only NASA Flight Quality (NFQ) rats and monkeys will be utilized for crew member training and flight activities. The NFQ criteria for rats are given in Table 1, for squirrel monkeys in Table 2, and for macaques in Table 3. The risk of amphibian zoonosis is minimal, therefore no special certification is required.

3. Other animal species proposed for flight experiments will be considered by the JSC IRB on an individual basis.

4. The following general guidelines will be followed where applicable:

   A. STANDARD MICROBIOLOGICAL PRACTICES

      1. Work surfaces will be decontaminated with a suitable disinfectant before and after use.

      2. All waste liquids, solids, tissues, syringes and needles will be placed in durable, leakproof, puncture-resistant, sealed containers for eventual autoclaving, incineration, or other appropriate decontamination/disposal procedure post-training, post-simulation or postflight. Such materials will not be transported between the animal investigation area and crew living quarters.

      3. Hypodermic needles and syringes shall be used only for the parenteral injection or aspiration of fluids from laboratory animals and diaphragm bottles. Only needle-locking syringes or disposable needle syringe units (i.e., the needle is integral to the syringe) are to be used for the injection or aspiration of fluids. Needles should not be bent, sheared or removed from the syringe following use. Needles should not be replaced in the plastic sheath or guard prior to disposal. Needle and syringe should be promptly placed in puncture-proof container for eventual decontamination, preferably by autoclaving, before final discard.

4. Personnel will use appropriate antiseptic wet wipes or other available means for cleaning hands after handling animals, when departing the laboratory, and especially before eating.

5. Laboratory coat (or equivalent) will be worn when animals are handled.

B. ANIMAL CERTIFICATION

1. Animals will be certified NFQ by the supplier for the proscribed organisms listed in Tables 1 , 2, and 3. The rats will be housed together in pairs in filtered cages. One animal of each pair will be sampled for microbial culture screening 72 hours prior to crew contact. Preliminary results will be available in 24 hours and definitive results in 72 hours. The crew will not be exposed to either animal in a single cage if the sampled animal cultures are positive for a proscribed organism. Rat viral serology will be completed two weeks prior to crew exposure according to established protocols.

2. The monkeys will be screened for proscribed organisms at six-month intervals. The flight animals selected will have viral serology screening completed one month before use and will be cultured for proscribed bacteria 96 hours prior to crew contact. All microbiological test results will be forwarded to the JSC IRB as part of the Operational Readiness Review (ORR).

3. NFQ certified squirrel monkeys will at all times be housed in isolation apart from other non-certified non-human primates. The isolation quarters will be provided with a nonrecirculating type ventilation system to preclude contamination from other animals. Room entry will require shoe covers in addition to the standard outerwear (lab coat, mask, gloves).

C. RESEARCH ANIMAL HOLDING FACILITY (RAHF) AND GENERAL PURPOSE WORK STATION (GPWS) IN-FLIGHT GUIDELINES

1. With the improved integrity of animal enclosures and associated flight procedures, THE ROUTINE USE OF LABORATORY ATTIRE IS NOT REQUIRED.

   If anomalous situations should develop which produce free contaminants, all crewmembers will use suitable protective measures (viz., NIOSH-approved respirator) until the particular experiment or procedure is terminated and the contaminant is satisfactorily removed from the spacecraft. This precaution is necessary in the closed microgravity environment, since contamination does not remain localized in the continuous atmosphere of spacecraft.

Particular care should be exercised during the following procedures:

a. Rats: Waste tray and food canister changeout; cage removal; condensate bottle changeout; GPWS operations involving animals.
b. Squirrel monkeys: Waste tray changeout; urine canister changeout; food canister changeout; blood sample collection.

2. High Efficiency Particulate Air (HEPA) filtration system of the RAHF and GWPS will remove more than 99% of all particles greater than 0.3 micrometers.

3. Biological samples from animals shall not contaminate the spacecraft or crew at any time during collection, transport and storage procedures.

4. Animals transported between the RAHF and GPWS must be enclosed in a carrier.

5. Equipment and procedures for the housing, transport, and experimental protocol must preclude any possibility of animal escape into the spacecraft.

TABLE 1. NFQ CRITERIA FOR RATS

MICROORGANISM	VERIFICATION PROCEDURES
BACTERIA:	
Bacillus piliformis	Liver (Invoke with Cortisone) (Microscopic Examination)
Campylobacter sp.	Fecal Culture
Clostridium tetani	Fecal Culture
Corynebacterium kutscheri	Oral and Nasal Cultures
Leptospira sp.	Urine Culture
Pasteurella multocida	Oral and Nasal Cultures
Salmonella enteritidis	Fecal Culture
Staphylococcus aureus	Skin Culture
Streptobacillus moniliformis	Oral Culture
Streptococcus pneumoniae	Oral and Nasal Cultures
Streptococcus pyogenes	Oral and Nasal Cultures
Spirillum minus	Oral Culture
ECTOPARASITES:	
Fleas:	
Xenopsylla cheopis	Skin (Clinical Inspection)
Xenopsylla segris	Skin (Clinical Inspection)
Nosopsyllus fasciatus	Skin (Clinical Inspection)
Lice:	
Liponyssus bacoti	Skin (Clinical Inspection)
ENDOPARASITES:	
Hymenopepis nana	Fecal (Microscopic Examination)
FUNGI:	
Microsporum sp.	Skin (Clinical Inspection)
Trichophyton mentagrophytes	Skin (Clinical Inspection)
PROTOZOAN DISEASES:	
Entamoeba histolytica	Fecal Culture
Encephalitozoon cuniculi	Urine Culture
Pneumocystis carinii	Urine Culture
VIRUSES:	
Hantaviruses	Serology
Lymphocytic choriomeningitis virus	Serology
Poxvirus(es)	Serology
Rat parvoviruses	Serology
Rat Rotavirus-like agent	Fecal (Enzyme Immunoassay)
Rat coronavirus	Serology
Sialodacryadenitis virus	Serology
Sendai virus	Serology

TABLE 2. NFQ CRITERIA FOR SQUIRREL MONKEYS

MICROORGANISM	VERIFICATION PROCEDURES
BACTERIA:	
Campylobacter sp.	Fecal Culture
Leptospira sp.	Urine Culture
Mycobacterium tuberculosis	Skin Test and Chest X-Ray
Pasteurella multocida	Oral and Nasal Cultures
Salmonella sp.	Fecal Culture
Shigella sp.	Fecal Culture
Streptococcus pneumoniae	Oral and Nasal Cultures
Streptococcus pyogenes	Oral and Nasal Cultures
ENDOPARASITES:	
Acanthocephalans	Feces (Microscopic Examination)
Entamoeba histolytica	Feces (Microscopic Examination)
Hemoprotozoa	Blood (Microscopic Examination)
Strongyloides	Feces (Microscopic Examination)
Trichomonas	Oral (Microscopic Examination)
FUNGI:	
Microsporum sp.	Skin (Clinical Inspection)
Trichophyton sp.	Skin (Clinical Inspection)
VIRUSES:	
Herpes tamarinus	Serology
Herpesvirus saimiri	Serology
Lymphocytic choriomeningitis virus	Serology
Rabies	Central Nervous System signs; follow-up by fluorescent antibody exam of brain tissue

TABLE 3. NFQ CRITERIA FOR MACAQUES

MICROORGANISM	VERIFICATION PROCEDURES
BACTERIA:	
Campylobacter jejuni	Fecal Culture
Mycobacterium tuberculosis	Skin Test and Chest X-Ray
Pasteurella multocida	Oral and Nasal Cultures
Salmonella sp.	Fecal Culture
Shigella sp.	Fecal Culture
Streptococcus (Diplococcus) pneumoniae	Oral and Nasal Cultures
Yersinia enterocolitica	Fecal Culture
Yersinia pseudotuberculosis	Fecal Culture
FUNGI:	
Microsporum sp.	Skin (Clinical Inspection)
Trichophyton sp.	Skin (Clinical Inspection)
PARASITES:	
Ascaris lumbricoides	Fecal (Microscopic Examination)
Balantidium coli	Fecal (Microscopic Examination)
Entamoeba histolytica	Fecal (Microscopic Examination)
Enterobius hominis	Fecal (Microscopic Examination)
Trichuris sp.	Fecal (Microscopic Examination)
Giardia sp.	Fecal (Microscopic Examination)
Hymenolepis nana	Fecal (Microscopic Examination)
Strongyloides sp.	Fecal (Microscopic Examination)
Trichomonas hominis	Fecal (Microscopic Examination)
SPIROCHETES:	
Leptospira sp.	Urine Culture
VIRUSES:	
Ebolavirus	Serology
Herpesvirus simiae (B virus)	Serology
HIV, SIV	Serology
Lymphocytic choriomeningitis	Serology
Monkeypox	Serology
Rabies	Central Nervous System signs; follow-up by fluorescent antibody exam of brain tissue
Rubeola (Measles)	Serology
SRV-1, SRV-2	Serology
STLV-I	Serology
Tanapox virus group	Serology
Yaba	Serology

IRB Guidelines Regarding In-flight Electrical Standards Associated with Bioinstrumentation to be Used for In-flight Investigative Monitoring of Shuttle Crewmembers

Bioinstrumentation systems shall be designed to limit, to safe levels, electrical shock currents that could flow through an instrumented crewmember as a result of contact with available voltage sources in crew bays, power cords, and extravehicular activity umbilicals or failures within the bioinstrumentation itself.

For voltage sources or power supplies using frequencies from d.c. to 1kHz, nominal subject leakage currents for bioinstrumentation systems utilizing indwelling catheters shall not exceed 10μA. There is insufficient data in the literature to indicate a **Critical Hazard** level with respect to indwelling catheters. Electric currents in excess of 20μA, conducted via an indwelling catheter, shall be considered a **Catastrophic Hazard** and shall be controlled as such.[1] For voltage sources or power supplies using frequencies above 1kHz, these values shall be multiplied by the numerical value of the frequency (in kilohertz), but may not exceed 1000μA.[2]

For voltage sources or power supplies using frequencies from d.c. to 1kHz, nominal subject leakage currents for bioinstrumentation systems utilizing body surface electrodes (ECG, EMG, EOG, etc.) shall not exceed 100μA (a.c. or d.c.).[3] Electric currents in excess of 500μA, applied externally, shall be considered a **Critical Hazard** and shall be controlled as such.[4] Electric currents in excess of 1000μA, applied externally, shall be considered a **Catastrophic Hazard** and shall be controlled as such.[5, 6] For voltage sources or power supplies using frequencies greater than 1kHz, these values shall be multiplied by the numerical value of the frequency (in kilohertz), but may not exceed 5000μA.[2]

Bioinstrumentation intended to apply electrical currents to crewmembers (e.g., neuromuscular stimulators etc.) shall be evaluated for maximum applied electric current on a case by case basis.

In cases where a crewmember will be instrumented with multiple biomedical instrumentation systems, consideration shall be given to possible interaction, nominal or in the event of failures, between the different instruments such that these requirements are not exceeded by the interaction.

RECOMMENDATION NOTES:

1) The 10μA current limit for isolated patient connections, as set by ANSI/AAMI includes a safety factor of 2 with respect to a minimum fibrillation threshold of 20μA for canines. Based on a human study reported in the Medical Journal of Australia (Watson et al., 1976), "It is unlikely that ventricular fibrillation will be induced with currents of much less than 60μA as the lower 99% confidence limit was above 65μA."

2) Increased nominal subject leakage current limits for frequencies above 1kHz are consistent with ANSI/AAMI, NFPA 99, and IEC 601-1.

3) In some cases where surface electrodes were worn for long periods of time, an electrolytic reaction between low levels of d.c. electrical current and skin may have caused irritation and/or mild blistering of the skin. 100μA is the allowable value of patient leakage current under no-fault conditions according to the IEC 601-1. The 50μA risk current limit designated by ANSI/AAMI includes a safety factor of 10 with respect to the minimum threshold of perception (500μA) for large contact areas of dry intact skin and a factor of two with respect to the threshold of perception (100μA) for breached skin or mucus membrane.

4) Although 500μA may be perceptible, a study performed by Underwriters Laboratories Inc. (Stevenson, 1969) indicated that 500μA was not likely to cause a hazardous startle reaction. A Canadian study has shown that 500μA applied to chest electrodes caused enough irritation that the subjects wearing the electrodes eventually removed them. 500μA is the maximum allowable level of current, given a single fault condition, according to the International Electrotechnical Commission (IEC 601-1).

5) 1000μA is well below the level of electric current required to cause a thermal burn, respiratory arrest, or cardiac fibrillation; however, this level of current may be high enough to startle an instrumented crewmember and possibly cause a secondary injury. "Thresholds of (cardiac) stimulation with a large-area chest electrode were measured typically between 40 and 70mA with a minimum value of 20mA in test of humans" (Zoll et al., 1985). "60Hz fibrillation thresholds for 200-mm sq chest on dogs averaged 6[illegible]mA" (Roy et al., 1986).

6) In situations where a crewmember is wearing bioinstrumentation and operating in a captive environment (i.e., EMU suit or LES), long-term exposure to skin irritation or mild blistering of the skin may impair a crew member's ability to perform his/her in-flight functions. In light of this possibility, 500μA shall be considered a catastrophic hazard for situations in which a crewmember is operating in a captive environment.

Summary Table

EQUIPMENT TYPE	FREQUENCY BAND	
INDWELLING CATHETERS	d.c. < $f \leq$ 1kHz	1kHz < f
Nominal Current Limit (Inom)	10μA	$I_{nom} = f$(kHz) x 10 ≤ 1000μA
Critical Current Limit (Icrt)	N/A	N/A
Catastrophic Current Limit (Icat)	20μA	$I_{cat} = f$(kHz) x 20 ≤ 1000μA
SURFACE ELECTRODES	d.c. < $f \leq$ 1kHz	1kHz < f
Nominal Current Limit (Inom)	100μA	$I_{nom} = f$(kHz) x 100 ≤ 5000μA
Critical Current Limit (Icrt)	500μA	$I_{crt} = f$(kHz) x 500 ≤ 5000μA
Catastrophic Current Limit (Icat)	1000μA	$I_{cat} = f$(kHz) x 1000 ≤ 5000μA
Catastrophic Current Limit (Captive Environment)	500μA	$I_{cat} = f$(kHz) x 500 ≤ 5000μA